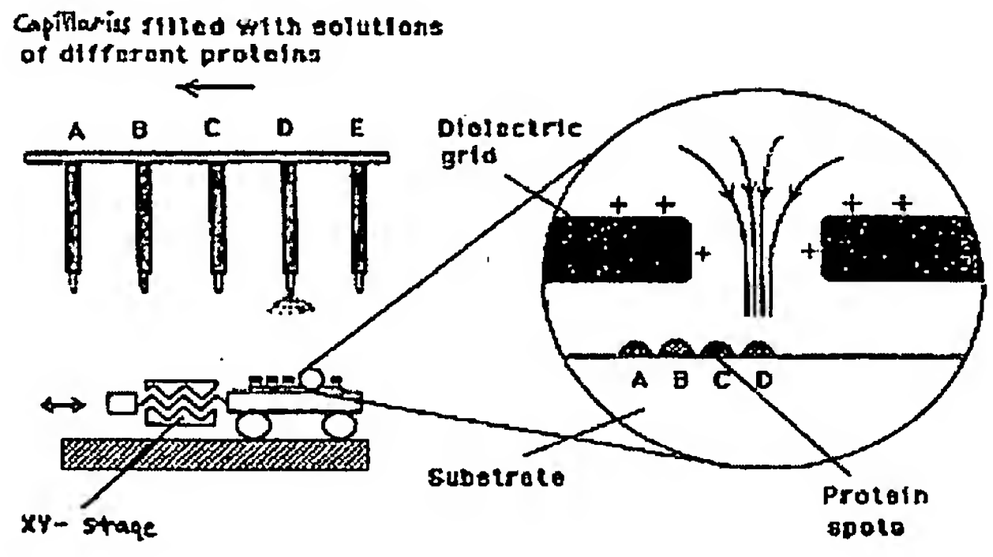
ELECTROSPRAYING SOLUTIONS OF SUBSTANCES FOR MASS FABRICATION OF CHIPS AND LIBRARIES

Patent number: JP2002511792T
Publication date: 2002-04-16
Inventor:
Applicant:
Classification:
- international: ***B01J19/00; B05B5/025; C07B61/00; G01N33/543; G01N33/545;*** **B01J19/00; B05B5/025; C07B61/00; G01N33/543; G01N33/544;** (IPC1-7): C12M1/00; C12N15/09; B05B5/025; B05B12/00; B05D1/04; B05D5/12; C07B61/00
- european: B01J19/00C; B05B5/025A; C07B61/00L; G01N33/543; G01N33/545; Y01N6/00
Application number: JP19990504841T 19980619
Priority number(s): US19970050274P 19970620; US19970055287P 19970813; WO1998US12768 19980619

Also published as:
WO9858745 (A1)
WO9858745 (A1)
EP0988112 (A1)
EP0988112 (A1)
CA2294449 (A1)
more >>

Abstract not available for JP2002511792T
Abstract of corresponding document: **WO9858745**

A method of fabricating deposits of non-volatile substances, including biomacromolecules, in the form of spots and films on a substrate surface by electrospray, where the deposits are used to determine the interaction of the deposited non-volatile substances to other substances. Also included in this method is the mass fabrication on a single chip of an array of single and multicomponent microsamples.



1. JP,2002-511792,A

* NOTICES *

1.This document has been translated by computer. So the translation may not reflect the original precisely.
2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

CLAIMS

[Claim(s)]
1. deposition of nonvolatile matter which has biological functions and/or biological activity the approach of manufacturing an object on a base -- it is -- biological functions -- and/or, biological electrostatic atomization of the solution of the activity matter is carried out -- making -- biological functions -- and/or, biological What [has the step which makes the nonvolatile matter which has activity deposit on a base front face] .
2. said step which carries out electrostatic atomization -- biological functions -- and/or, biological The step to which electrostatic atomization of the solution of said nonvolatile matter which has activity is carried out, and ****** Matter which has biological functions and/or biological activity for the matter by which fog was carried out Method according to claim 1 of having the step which is carried out and is made to deposit on a base front face.
3. Said electrostatic atomization step and a deposition step deposit on a base front face. Claim which has the step which makes the electrostatic charge of the matter by which electrostatic atomization was carried out carbonate Approach given in a term 2.
4. Said base is the dielectric layer which is made of the conductive matter and was prepared on the base. Electrostatic [of the matter by which electrostatic atomization was carried out by making conductivity increase locally] are . Method according to claim 3 of having the step which makes a charge carbonate.
5. said dielectric layer -- from the photoconductivity matter -- it can do -- **** -- this photoconductivity insulating layer -- light local [in the conductivity of said dielectric layer] by irradiating locally -- an increment -- Method according to claim 4 of having a **** step.
6. By pouring in the carrier which carried out the electric charge from the external source of supply, it is said dielectric. A layer is locally made into conductivity and the carrier which carried out the electric charge is locally injected into said dielectric layer. Step to which the conductivity of said dielectric layer is made to increase locally by carrying out The approach according to claim 4 of having.
7. Said dielectric layer is made of the pyroconductivity matter, and is about said dielectric layer. Step to which the conductivity of said dielectric layer is made to increase locally by becoming hot The approach according to claim 4 of having.
8. Make conductivity increase locally by opening a hole in said dielectric layer. Method according to claim 4 of having a step.
9. Base of nonvolatile matter which has biological functions and/or biological activity SA of the area to which the size of the deposit on a front face made conductivity increase locally Approach [quite smaller than IZU] according to claim 4.
10. Biology which said deposition step mentioned above in the location where it was beforehand set on the base About the deposit of the matter which has the-like function and/or biological activity, it is control of an electrostatic field. Claim which is the step made to form in the gestalt and configuration which were defined beforehand in the bottom Approach given in 3.
11. the electrostatic field where plurality was limited is generated on a base -- making -- two or more biological functions -- Coincidence is made to deposit on a base the nonvolatile matter which has **/or biological activity. Method according to claim 4 of having a step.
12. It is said electrostatic atomization SU, moving the location of the electrostatic field where said plurality was limited. The approach according to claim 11 of repeating tetraethylpyrophosphate and a deposition step.

13. Various ** in which each has biological functions and/or biological activity About the various solutions containing volatile matter, they are said electrostatic atomization step and a deposition step. The approach

according to claim 12 of making it deposit repeatedly.
14. Object by which has arranged the guard shield plate of a dielectric around a capillary tube, and electrostatic atomization was carried out Method according to claim 2 of enclosing quality and having the step which prevents distribution.
15. It is a publication to claim 14 which the hole is opening to the guard shield plate of said dielectric. Approach.
16. Step which prepares a convergence ring in the surroundings of the base area to which conductivity was made to increase The approach according to claim 4 of having.
17. Give potential to said convergence ring and the greatest rate of all currents is a base from a capillary tube. SUTETSU which enables it to attain the stable electrostatic atomization as lets it pass and flows Method according to claim 16 of having PU.
18. Non-volatile object which has the biological functions and/or biological activity which were deposited Approach according to claim 3 quality has the step which forms a film.
19. Non-volatile object which has the biological functions and/or biological activity which were deposited Approach according to claim 18 said nature film has the form which is not round.
20. Step which puts a conductive or half-conductive layer on a base before electrostatic atomization He is Phi have and according [a conductive or half-conductive layer] to electrostatic atomization by this. Method according to claim 18 of offering the front face for making RUMU deposit.
21. The above of the nonvolatile matter which has biological functions and/or biological activity It also has the step which makes a film exfoliate from a conductive or half-conductive layer. Approach according to claim 20.
22. Claim 2 in which said conductive layer contains the meltable matter chemically or physically Approach given in 1.
23. The approach according to claim 22 said conductive layer contains a hydrophilic polymer.
24. The approach according to claim 2 the solution by which electrostatic atomization was carried out also contains a stabilizer.
25. The nonvolatile matter which has biological functions and/or biological activity is **. The approach according to claim 2 of being the Daisei object molecule.
26. The nonvolatile matter which has biological functions and/or biological activity is included. It is electrostatic atomization, without carrying out electrostatic atomization of the solution from a capillary tube, and causing corona discharge for a capillary tube. It is a publication to claim 2 which has the step set as sufficient potential for making it function. Approach.
27. ** which also has the step to which the crosslinking bond of the sample of the deposited huge biomolecule is carried out Approach given in **** 25.
28. The approach according to claim 27 huge biomolecule is protein.
29. To claim 28 in which the solution by which electrostatic atomization was carried out also contains the protein stabilizer of fusibility The approach of a publication.
30. Flush a protein stabilizer from the protein film which carried out the crosslinking bond, and it is porous **. Method according to claim 29 of also having the step which obtains a white matter film.
31. Contact the protein film and reactant which were deposited and create a uniform film. Method according to claim 28 of also having the step to carry out.
32. Said reactant is the approach according to claim 31 of being a steam.
33. About said protein, the magnitude of a cluster is the protein between 5 to 50 nanometers. It is an account to claim 28 which has the step made to deposit as a minute cluster of a nature molecule. The approach of **.

34. Perform an electrostatic atomization step in about 10 to 40% of ambient atmosphere of a humidity requirement. Approach according to claim 33.
35. It is the protein film generated by the approach according to claim 33, and is a bank. Although the minute cluster of the protein molecule which carried out the product is not combined completely, it is ** to high density. Said film is tea between sufficient clusters to carry out ** and for ligand permeate. What has flannel.
36. un-volatilizing [said whose solution has biological functions and/or biological activity] the sex matter -- containing -- the conductivity of said solution -- about 500micro less than siemens/cm it is -- approach according to claim 2.
37. Step at which the current which passes a capillary tube is maintained in the range of 50nA(s) from about 1 The approach according to claim 26 of having.

38. The approach according to claim 25 said huge biomolecule is a nucleic-acid molecule.
39. Base with which the front face which the film by which electrostatic atomization was carried out deposits has low conductivity The approach according to claim 18 of being a front face.
40. Claim whose front face which said film by which electrostatic atomization was carried out deposits is porosity Approach given in a term 39.
41. Electrostatic atomization was carried out, and while being both the deposited matter, electrostatic atomization was carried out and it deposited. SU which makes the reaction between the molecules between the matter and the molecule which exists on a base prevent Approach also containing tetraethylpyrophosphate according to claim 2.
42. Protein Phi formed on the base by carrying out electrostatic atomization of the protein solution It is RUMU, and is the thickness of the range of 0.4 to 20 microns, and he is Phi. That in which the thickness of RUMU has less than **10% of homogeneity.
43. Said protein film is a protein molecule from the magnitude of 5nm to 50nm. Protein film containing a cluster according to claim 42.
44. Make high density fill up with a protein molecule cluster, without making it join together completely, and it is protein. A nature film has a channel between sufficient clusters for ligand to permeate. **, protein film according to claim 43.
45. It has biological functions and/or biological activity on a base and said base. It is a sample containing the deposit of a large number to which electrostatic atomization of the matter of ****** was carried out, and is each deposition. That whose magnitude of an object is less than 7 microns.
46. It is the deposit of various matter which carried out electrostatic atomization per [200 and 0] 1 inch square. Sample according to claim 45 made to form by the consistency exceeding 00.
47. Nonvolatile Matter Which Has Biological Functions and/or Biological Activity is Included. By Carrying Out Electrostatic Atomization of the Solution Biological functions and/or biological ** With the equipment which makes the sample of the nonvolatile matter which has a sex deposit on the deposition area of a base It is. Said equipment In the space filled with gas, they are biological functions and/or biology from a solution. ********** which generates spraying containing the nonvolatile matter which has the-like activity of a charged particle **, It is a base table by irradiating alternatively or not irradiating. On the deposition area of a field The 1st potential which draws a charged particle, and except for deposition area Feeling of the electrical and electric equipment which generates the 2nd potential which does not draw a charged particle on the area on the front face of a base Thing including a light-means.
48. Equipment containing the 1st electrostatic equipment connected to said base according to claim 47 .
49. Claim containing the mask which kept spacing in the front-face bottom of said base, and has been arranged Equipment given in 47.
50. Since a mask is passed and the deposition area on a base is irradiated by the pattern of light Equipment including the light source according to claim 49.
51. Nonvolatile Matter Which Has Biological Functions and/or Biological Activity is Included. By Electrostatic Atomization of Solution It has biological functions and/or biological activity. It is equipment which makes the sample of ********** deposit on the deposition area of a base. Said equipment the inside of the space filled with gas -- the biological functions from said solution -- and/or -- ****** which generates spraying of the charged particle containing the nonvolatile matter which has biological activity With misty equipment It is ** to the 1st potential which draws a charged particle for the base front-face top near the deposition area. 1st electrostatic equipment which it has, It is held at the potential which repels a charged particle, and spacing is kept above the base front face and it arranges. Mask which has the hole which it is carried out [hole], it is located [hole] above the deposition area, and passes that It contains. It considers as the ratio to which the magnitude of the hole of said mask was beforehand set to said distance. -- the part in which said hole has said the ratio and the 1st potential which were defined beforehand, and 2nd potential -- ** a place is made to generate and a charged particle is converged by this -- making -- deposition area -- said -- a hole -- What [was constituted so that ** may also become small]
52. It is said ** when said mask takes in the charge from a charged particle. Equipment according to claim 51 which reaches the potential of 2.
53. The front face of a non-conductive ingredient adsorbs a charged particle, and said 2nd potential is a charged particle. The bottom which repels spraying, equipment according to claim 52.
54. Equipment according to claim 53 said mask is made of the non-conductive ingredient.
55. Equipment according to claim 53 said mask is made of the conductive ingredient.
56. Equipment according to claim 51 said mask is made of the conductive ingredient.

57. Claim 56 containing the 2nd electrostatic equipment which makes said mask hold to the 2nd potential Equipment of a publication.
58. Other parts on the base front face after making a charged particle deposit on a certain deposition area are degrees. Mask to which a mask is moved in parallel to a base so that it may become deposition area Equipment containing migration equipment according to claim 51.
59. Include a means to vibrate a capillary tube on said mask, during migration of said mask. Equipment according to claim 58.
60. Equipment according to claim 59 with which said mask includes the array of a hole.
61. Describe above only spacing fixed almost in parallel to a base front face after depositing each matter. Equipment including the means to which a mask is moved according to claim 59.
62. Move so that the pattern of a spot can form the array of the substrate of two or more components. Equipment according to claim 59 which made distance shorter than spacing with the next hole.
63. the same polar potential as the charged particle which separates from a capillary tube tip -- having -- a capillary tube tip -- almost -- It is located in the same level and an electrostatic atomization discharge zone is enclosed with the charge which repels a charged particle. Claim 51 which prevents the diffusion in electrostatic atomization by this including a protect ring Equipment of a publication.
64. Set on a base front face by the flow of the reversed-polarity ion from corona discharge, and it is a period. Equipment including the means made to regrout a charge-like according to claim 51.
65. Include the array of a micro electrode in the covered chamber, and it is ** periodically. Equipment [equipped with the means made to regrout a load] according to claim 64.
66. Claim containing the non-conductive guard shield plate arranged around the spraying matter Equipment given in a term 51.
67. Equipment according to claim 66 with which the hole sticks to said guard shield plate.
68. Equipment according to claim 66 with which said guard shield plate is trapezoidal shape .
69. Equipment according to claim 66 with which said guard shield plate has become cylinder-like .
70. Equipment according to claim 51 whose hole of said mask is not round.

[Translation done.]

DETAILED DESCRIPTION

[Detailed Description of the Invention]
Display about the application of a chip and the matter solution in extensive manufacture of a library which carries out electrostatic atomization relation This application is what asserted the priority based on the U.S. caveat application 60th for which it applied to the U.S. caveat application 60th / No. 050 or 274, and August 13, 1997 which were submitted on June 20, 1997 / No. 055 or 287, and all these contents are included by this application.
Field of background invention of invention This invention relates to the technique which deposits protein and the sample matter containing biomolecule like DNA as a specific configuration or a specific pattern on a base front face, and the technique which is made to dry the solution of these matter quickly and forms a slight quantity of an aggregate.
Explanation of a technical background He makes a solution or a liquid spray electrostatic, and is trying to generate the electrified ion and a cluster, and the minute electrified drop in an electrostatic atomizing process (electrospray). If the liquid or solution of the matter which should be deposited is introduced into a capillary tube (or array of a capillary tube) and the high voltage is impressed, a liquid or a solution will be in an unstable condition, and a liquid and a solution will be typically distributed as an electrified drop with a diameter of about 0.5-2 microns the diameter of 0.3-20 microns. According to electrostatic reaction force, the electrified drop is quickly separated from the tip of a capillary tube. When the vapor pressure of a solvent is low enough, in the stroke to a base front face, a minute drop is dried and the size of a drop reaches the Raleigh limitation (Raleigh limitation) of an electrostatic balance. Then, a minute drop follows a series of attenuation processes, and an electrostatic field increases to the level on which size can become about 10-20 nanometers, and the ionized solvent molecule can evaporate. Furthermore, a solvent is removed from the solution molecule ionized while passing the dry gas. Thus, if rapid evaporation advances, all the solute components of a drop will be condensed and will serve as a minute cluster (nano cluster) (drawing 1).
When the solvent of low vapor pressure, for example, an electrostatic atomizing process of the solution of a thing like water, is the electrostatic atomization in the ambient atmosphere containing a lot of solvent steams, or when the source of electrostatic atomization is a short distance from the base front face for deposition, a drop will not evaporate all solvents, and will not be decreased completely, and will reach a base. This approach is called a wet electrostatic atomizing process.
An volatile solvent is used and deposition of the molecule or cluster charged in the dry type electrostatic atomizing process when the distance of the condition that the solvent partial pressure in a gas is low or a base front face, and the source of electrostatic atomization was long arises.
Therefore, the matter will accumulate with the gestalt of the ionized molecule which melted into the electrified minute drop or the solvent, or was dried according to this electrostatic atomization phenomenon, or a minute cluster. A minute cluster or fiber is generated by the electrostatic atomizing process using liner polymer. The configuration of a deposit can be adjusted by changing the stroke of the electrified chemical species, and a rate. This accommodation becomes possible by choosing appropriately accommodation of the vapor pressure of an ambient atmosphere, and the concentration of a solvent and a solution.
One of the earliest application of an electrostatic atomizing process is generation of the thin activity source of supply for radioactivity measurement. The collimator which brings about electrostatic convergence was introduced in this application (1973 besides Robinson, 1965, and Van Dear EIKU (van der Eijk)). Furthermore, BURUNNINKUSU etc. is indicating the disk made from PUREKISHI glass (plexiglass) which what carried out electrostatic atomization passes and which the hole opened at the core, before reaching a base or a collector (1961). In order that Van Dear EIKU etc. may obtain the source of supply of the thin radioactive substance with the area specified clearly (1973), it is indicating that such a mask can be

used. Furthermore, by the approach using the Teflon first announced by BURUMUBAGU etc. (1962), the product of the thin source of supply of the radioactive substance clearly smaller than the diameter of the hole of the mask mentioned above can be formed.
The ion source of supply for the mass spectrometries of application of other electrostatic atomizing processes, for example, electrostatic coating, a insect-killing spray, and biomolecule etc. is indicated by Michelson (1990). Thus, the electrostatic atomizing process of biomolecule develops in order to measure the description on use of a mass spectrometry especially the molecular mass of biomolecule, a noncovalent interaction, and structure. It was most important for having been found out on another application of the electrostatic atomization of biomolecule to hold the perfect structure of protein ion and to hold a noncovalent interaction. For example, using DNA and the protein molecule deposit in which electrostatic atomization was carried out by the research in an electrostatic atomization mass spectrometry in performing imaging by tunnel scan spectrometry was promoted (1993 besides 1992 besides SANDATTO, and Morozoff). Although SANDATTO etc. carried out electrostatic atomization of the solution of a direct DNA molecule on the golden base (1992), Morozoff etc. inserted the protective plate containing an ion channel (1993) between the bases and the sources of electrostatic atomization which should deposit protein ion. After the accelerated protein ion moreover collides with a mica or a graphite, it is often written to reference that the both sides of protein ion and a collision side are destroyed (1996 besides 1994 besides Layman, and SHURIVAN).
It has been developed when forming protein or other biomolecules in a predetermined pattern uses the conventional various techniques. For example, it is the manufacturing technology (1988 besides NAKAMOTO) of the usual electrical circuit which uses pipetting (1996 besides Sharon), screen-stencil (1994 besides the heart), ink jet deposition (1992 besides Newman) or photoresist, and lift-off technique of the minute drop by the robot with which computer control was carried out. Moreover, although the approach of depositing electrically from a solution on the array of the micro electrode assembled in advance in the biosensor technique was also developed (1994 besides 1994 besides a strike, and Johnson), most application of the electric depositing method is limited to protein, and preparation of a base and positioning of a micro electrode take a complicated procedure to it. Moreover, deposition of the protein from the solution to a micro electrode top has a possibility of doing damage to a protein molecule on the interface of a solution-metal according to direct oxidation and/or localization of pH accompanying the electrochemical reaction on an electrode. These electric depositing methods are few, or can adjust the consistency and structure of a film to deposit with some parameters. By the electric depositing method from a solution, after carrying out the crosslinking bond of the sample, conversion of the electrode surface cannot be carried out by the water-soluble polymer so that it can dissociate from a base easily.
Although the shadow masking technique was announced recently as an approach of forming the pattern of the polypeptide fiber created by electrostatic atomization on a silicon front face, the surface adhesion force of a cell is made to increase (1996 besides the buchu (Buchko)). However, use of the conditions of this electrostatic atomizing process, i.e., the formic acid as a solvent, does not suit maintenance of the functional activity of a large majority of huge biomolecules, and the three-dimensional structure. On the other hand, in use of shadow masking, a result in which electrostatic atomization of a lot of matter is carried out, and it is lost on a mask is brought. There were not protein by which electric deposition was carried out, and data reliable about whether the functional property of a DNA molecule is held.
It was shown clearly that the DNA molecule a large number carried out [the DNA molecule] conversion deposits a chain etc. as a result of carrying out electrophoresis analysis of the plus imide DNA by which electric deposition was carried out on the stainless steel electrode which dried this in deposition of a DNA molecule (1996). Such conversion was not able to be discovered in the experiment which carries out the electric deposition of the DNA as a drop of buffer solution.
Robinson (1966) released what attached two annular copper disks to the surroundings at the tip of the electrostatic atomization named the protect ring, i.e., a collimator.
Belt RINI etc. released the hole which carried out the truncated cone form where the upper and lower sides were reversed for the inner surface (1965).
BURUNNINKUSU etc. announced what opened one hole in the PUREKISHI glass disk set so that a base might be covered on the base of the sheet metal of aluminum (refer to 132 - 133 pages in 1961). This base rotates and is aligning that revolving shaft and the one aforementioned hole.
This equipment secures distributing the spraying matter over homogeneity into the part which is not covered. He can understand two things from this. It is 1st rotating a base so that a spraying object's may be distributed over homogeneity since the spraying pattern from the tip of electrostatic atomization is uneven. I

hear that 2nd a PUREKISHI glass disk [/ else / BURUNNINKUSU] functions as a template of spraying spraying, and the covering part of a base is only covered rather and there is rather than the stroke of a charged particle is influenced by the electrostatic field. It should not expect to converge on the place which BURUNNINKUSU calls "the location defined appropriately", i.e., a clear boundary, electrostatic.
The channel of ion attaches Morozoff etc. in the center (1993) (please refer to p760 and drawing 2), and it has reported the instrument containing the plate with an electrode which became a double layer. The channel of the ion made from a plastic tube serves as a cone form. The potential difference is given between two electrode layers separated with the central insulation plate.
Recently, the manufacture approach of the biochip using a photograph chemical reaction is also developed by the group from whom a large number differ (U. 1991 besides 1994 besides 1995 besides 1993 besides the S. patent 4562157 and BASHA (Bhatia), and Prichard (Pritchard), and piece, and FODA (Fodor)). By these approaches, the front face which can be made to be able to perform various chemosynthesis of a living body polymer as a pattern contraction-ized on the dense base material using light, or can fix the protein which can be positioned with light, and DNA is supplied.
An optical mask method makes light go to the specific part on the front face which can be positioned with light, and it is used in order to bring about optical deprotection (photodeprotection) locally.
According to the manufacture approach of the biochip using a photograph optical reaction, deposition of each molecule which becomes a pattern takes at least three steps.
(1) Photoactivation on the base front face by the optical exposure to a specific part (optical deprotection).
(2) Put into the solution of the molecule which should deposit the activated base.
(3) Washing of the molecule which has not been combined (drawing 2).
These three steps are repeated whenever it deposits the new matter on a front face.
However, these advanced technology has many faults. There are the following in these faults.
(i) Since the number of the functionalized group who appears after an exposure is restricted, the total amount of the matter deposited on each spot is restricted.
(ii In each sedimentary cycle, it is necessary to put all front faces to the solution of the molecule which should be deposited.) For this reason, the result that some of these molecules are combined with the location (un-photoactivating) which is not irradiated in un-specifying will be drawn inevitably. This poses a problem protein and on the design of a pattern with a molecule complicated in addition to this.
(iii) others -- a pollution source is the interface of the solution with which the surface activity impurity always exists in abundance.
(iv) For light scattering protruded from the diffraction effect and the pattern space in an optical exposure, resolution falls and the cross contamination of a spot happens.
No quotation documents mentioned above were also mentioned as important data when judging the patentability of what kind of claim of this application while not being mentioned as what shows the advanced technology which relates to this invention closely. Although which the contents or date of bibliography is based on what has an applicant available at the time of application, they do not admit being completely exact.

Outline of invention Therefore, the purpose of this invention is conquering the defect of the above advanced technology.
This invention offers the approach of manufacturing the chip which contains the sample of two or more nonvolatile matter, for example, two or more samples, by deposition of electrostatic atomization. Such a sample is used in order to measure an interaction with other matter of the deposit of nonvolatile matter.
Furthermore, this invention offers how each manufactures the chip of a large number containing the sample of the molecule of the class of that one or more are biological or others to coincidence. There are many applications in such a chip. Especially a single component chip is used as an induction component which can renew a chemical sensor. Two or more component chip (library) is used for multiplex analysis of analysis of compound-izing (hybridization) of Micro ELISA (enzyme immunoassay) and a nucleic-acid molecule, sieving of effective enzyme inhibitor, etc. Both a microchip (each sample on a chip is the thing of a micron unit) and a macro chip (thing of Miri or a cm unit) are manufactured by the same technique. Such a macro chip is used for manufacture of the induction analysis kit of the diagnostic check for making allergen respond, i.e., the antibiotic of a microorganism, etc.
Moreover, this invention offers the efficient manufacture approach of protein and the minute sample of a DNA molecule which carried out cross coupling from the sample of a nanogram unit. Furthermore, the protein of the micro sample deposited by the electrostatic atomizing process and a DNA molecule film hold the functional property.

Furthermore, this invention offers even the equipment for sample manufacture of the nonvolatile matter by the electrostatic atomizing process as well as the sample product formed of the electrostatic atomizing process mentioned above.
Easy explanation of a drawing Drawing 1 is the diagram showing the electrostatic atomization process explaining the various conditions of the spraying matter in the various distance from the tip of the capillary tube of electrostatic atomization. The minute drop of a solution is superior in a wet zone, and the dry cluster and the dry ion are superior in a dry zone.
Drawing 2 illustrates the step of deposition of the molecule to the base top functionalized by optical positioning by the advanced technology.
Drawing 3 A and drawing 3 B are the diagrams showing the electrostatic concentration effect (drawing 3 A) and electric convergence (the electrostatic-lens effectiveness; drawing 3 B) in deposition of the charged particle which passed the hole of a dielectric mask by the electrostatic atomizing process.
Drawing 4 illustrates about the deposition (drawing 4 B) to the distribution of a charged particle by which passed the array (drawing 4 A) of the hole of a dielectric mask, and electrostatic atomization was carried out to many spots, and the conductive area which has irradiated light at the photoconductivity dielectric layer. Drawing 4 C is the diagram showing the sectional view of the base of drawing 4 B.
Drawing 5 A-5D passes the hole on a polypropylene mask (drawing 5 A) and a mask. The spot of the myoglobin deposited in the electrostatic atomization to the glass top covered in the conductive tin-oxide layer (drawing 5 B), The spot (drawing 5 C) of the coloring matter which passed and deposited the same mask on the mica into the damp ambient atmosphere, and the spot (drawing 5 D) of the coloring matter deposited on the dielectric layer of the photoconductivity irradiated by the diffraction pattern of a laser beam are shown.
Drawing 6 is the diagram showing manufacture and the separation process of a sample film.
Drawing 7 shows in diagram the deposition by the electrostatic atomizing process to the base cooled by liquid nitrogen.
Drawing 8 shows in diagram the use situation of the scanning-type/atomic force microscope about what the coordinate bond to the substrate of a protein spot is detected for by measuring the difference between the magnitude of the protein spot by the result of coordinate bond, and resiliency.
Drawing 9 shows extensive manufacture of the substrate of two or more components in diagram by the approach of moving the relative location to a base, after each matter passes the hole on a mask and electrostatic deposition is carried out at a base.
Drawing 10 A-10F show a series of six masks used in order to manufacture the combination of the library about a 6-mer oligonucleotide. This white part expresses the hole on a mask.
Drawing 11 shows the IMMOBILON-P (PVDF: poly vinylidene JIFURIORIDO) membrane filter of the porosity in which two or more component matrix of a large number which arranged the coloring matter spot of a different class was formed.
Drawing 12 A and 12B show the deposit (drawing 12 A) by the electrostatic atomizing process of a peroxidase solution, and the deposit (drawing 12 B) by the electrostatic atomizing process of an alkaline phosphatase solution to the damp IMMOBILON-P membrane filter top. A black point is accumulation of a peroxidase and the insoluble product by the enzyme reaction of alkaline FOSUTAZE. Moreover, a black point clarifies the location of the deposited enzyme on a membrane filter.
Drawing 13 shows the analysis result by the micro ELISA of the various protein antigens (the body, a bovine albumin blood serum, an ovalbumin, Homo sapiens hemoglobin) deposited on the IMMOBILON-P membrane filter by the electrostatic atomizing process. Moreover, these protein antigens are detected by the Homo sapiens albumin blood serum with an immunity enzyme technique the 2nd the 1st using the anti rabbit IgG (immunoglobulin G) molecule in which alkaline HOSUTAZE carried out the conjugated bond using the antibody of a rabbit with special virtue.
Drawing 14 A and 14B show the film (drawing 14 A) of the concanavalin A manufactured by the electrostatic atomizing process, and the film (drawing 14 B) of the alcoholic dehydrogenase extracted from the liver of a horse. A proteinic film passes the hole (0.8x0.2mm) of one rectangle on a mask, and deposits it on the auxiliary layer film of the conductive polymer beforehand deposited on the alm NIUMU electrode.
Drawing 15 A-15C is the vesicular structure (after making the image on the front face of a film deposit in dry type, it is acquired under a scanning force microscope (scanning force microscope).) of the Homo sapiens hemoglobin made to deposit by the electrostatic atomizing process. By "calcinating" drawing 15 A and a film shows (drawing 15 C) for the permeability of the film on which the bovine albumin blood serum was made to deposit by the electrostatic atomizing process improving fairly as compared with the film

which acquired changing to film structure as a result (the image of drawing 15 B expressing the structure after putting the same film into the damp ambient atmosphere), and a graph by the approach of drying the conventional protein solution. An axis of ordinate expresses with drawing 15 C the square of the distance from the front face of the protein film which became wet in the ambient atmosphere with which it became wet in case a coloring matter molecule permeated to the particle of uniform coloring matter. The data of the bromophenol blue in dry type [round head / of void] and a black dot express the data of the bromophenol blue in the film deposited by the electrostatic atomizing process. The rectangular head of void expresses osmosis of the Janus GreenB coloring matter in dry type, and a black rectangular head expresses osmosis of the Janus GreenB coloring matter in the deposition film by the electrostatic atomizing process. An axis of abscissa is penetration time.

Drawing 16 A-16C shows in diagram uniform distribution of the guard shield plate made from plastics of two types and the matter by which electrostatic atomization was carried out. This electric shielding plate is used for preventing that the matter by which electrostatic atomization was carried out swerves from a target base. In drawing 16 A, a trapezoid electric shielding plate centralizes a direct charged particle to the hole on a base or a mask. The design shown by drawing 16 B explains crossing to a large location and making homogeneity deposit the matter sprayed to the part of the shape of a cylinder surrounded by the wall of a mask. The electric shielding plate in these two kinds of designs can be made with the plastics with which the base material or the hole opened. In that it is easy for the direction of the latter design to separate the flow of air (wind) from the flow of a charged particle, it is advantageous, therefore concentration of the matter by which electrostatic atomization was carried out, and desiccation become easy. Drawing 16 C expresses the uniform distribution in the shelter inside of the shape of a cylinder made from plastics which is opening the hole which disagrees with distribution of the matter by which electrostatic deposition was carried out of a bell mold. The type of distribution of a bell mold is deposited without a shelter when the diameter of a cylindrical hole is smaller than the distance between base - capillary tubes. From a base, height of 55mm and a black dot express height of 43mm, and, as for the round head of void, a capillary tube expresses the deposition in 30mm, as for a rectangular head. The cylinder with which the hole with a diameter of 43mm opened is made of the nylon cloth (Florida, the small parts company make of the Miami rake, a CMN-1000-A mold, 1000-micron mesh size) of a single fiber.

Drawing 17 shows the coloring matter pattern of the macroscopic size manufactured by the electrostatic atomizing process of air-bleed assistance.

Drawing 18 A and 18B show the effectiveness of the current given to recovery of the specific activity over the alkaline phosphatase deposited under cane-sugar un-existing according to an electrostatic atomizing process, or cane-sugar existence (black dot) (round head of void), and thing and drawing 18 B to which drawing 18 A has an electrode in the interior of a capillary tube has an electrode in the exterior of a capillary tube. Weight equivalent to 50% of the protein which dried cane sugar is applied. An axis of ordinate expresses the ratio of the specific activity of the first solution, and the specific activity of the alkaline phosphatase deposit by the electrostatic atomizing process. The deposition by electrostatic atomization is carried out **5% in the state of relative humidity 65 flow-rate [solution] L/h of 6micro.

The array of a sample with the large ratio beside [height-] a deposit is formed of the electrostatic atomizing process of the protein with which drawing 19 A and drawing 19 B pass the hole of the polypropylene film of a deposit which illustrates a diagram (drawing 19 A) and a sectional view, respectively (drawing 19 B), and is used as a mask.

Drawing 20 A-20C illustrates three kinds of capillary tubes used as the ion source. Drawing 20 A shows the capillary tube of an external electrode, drawing 20 B shows the capillary tube of an internal electrode, and drawing 20 C shows the capillary tube of a liquid bridge (liquid bridge). In lead wire and 4, a glass capillary tube and 6 show the internal electrode of a tungsten, stainless steel, platinum, or gold, and, as for the glass capillary tube with which in the reference number 1 applied the tube made from plastics and 2 applied the silver layer, respectively, and 3, the tube made from stainless steel and 5 show a glass capillary tube, as for 7.

Drawing 21 illustrates the chamber used since protein is deposited on a microbalance in the example 11.

Drawing 22 shows the effectiveness of the sugar to recovery of the specific activity of the alkaline phosphatase after direct drying. The round head and black dot of void show the result of cane sugar and trehalose, respectively. Specific activity is proportional to the specific activity of an early solution.

Drawing 23 shows the effectiveness of humidity over recovery of the specific activity after the deposition by the electrostatic atomizing process of alkaline phosphatase. The specific activity of the sample made to deposit by the electrostatic atomizing process is proportional to the specific activity of an early solution. The

conditions of the deposition by the electrostatic atomizing process are +4kV, current 10-50nA, and flow rate L/h of 6micro in the capillary tube of an internal electrode.
Drawing 24 is the schematic diagram of the equipment of this invention.
Drawing 25 is the schematic diagram of the electrostatic atomization chamber shown by drawing 24 .
Drawing 26 is the perspective view of the capillary tube of an electrostatic atomization chamber.
Drawing 27 is the perspective view of the grid-like electric shielding plate of an electrostatic atomization chamber.
Drawing 28 is the perspective view of the convergence ring of an electrostatic atomization chamber.
Drawing 29 A is the sectional view of the guard shield plate of an electrostatic atomization chamber.
Drawing 29 B is the decomposition perspective view of the guard shield plate of an electrostatic atomization chamber.
Drawing 30 is the decomposition perspective view of the holder of a middle sample.
Drawing 31 is the perspective view of a sample holder.
Drawing 32 A is the transverse-plane schematic diagram of the 2nd suitable example of an electrostatic atomizing process at drawing 25 and this similar appearance.
Drawing 32 B is the detail drawing of drawing 32 A.
Drawing 33 is the decomposition perspective view of mask migration equipment.
the [of the electrostatic atomization chamber to which drawing 34 is similar with drawing 25] -- it is the diagram-front view of 3 suitable examples.
Detailed description This invention is developed in order to offer the manufacture approach of the deposit sample of the nonvolatile matter containing biomolecule (for example, protein, huge biomolecule like DNA), organism molecules (thing on an antibiotic and pharmaceutical sciences etc.), mineral matter, salts, inorganic colloid, etc. Biomolecule etc. serves as a specific configuration and an array, and is deposited.
This approach has the following advantages to the approach of the conventional biomolecule patternizing.
(1) There is no cross contamination of different spots like a photograph optical method, and there are not the whole chip front face and contact of a solution.
(2) Objectively [the ink jet method], it can deposit on coincidence at much chips, therefore processing is promoted. (3) (5) which can use the same technique as manufacturing (4) microchips which make manufacture of a smaller spot easy, and a macro chip as compared with the ink jet method since the size of a charged particle and a molecule is small therefore -- the inside of a certain gas -- setting -- and -- or deposition is performed using the liquid of a dielectric to the bottom of low temperature.
The mask of the array of the pattern of the hole (various forms) of one non-round shape or a hole is used for this approach. And this mask is inserted between the source of electrostatic atomization, and the base front face which a sample deposits. Thus, the electrified minute drop, a cluster, and ion will pass the array of the hole of a mask, or a hole, and will go to a base front face. Since many holes are in a mask according to the approach of this invention when a mask has the array of a hole, a separate spot can be formed as a matter of fact on a base front face at coincidence. The chip (library) of two or more components is formed in the bottom of each hole as a result by moving a mask after deposition of each compound.
Electric field are made locally and the approach of others which draw a charged particle is included within the limits of this invention. As for especially the conductivity of the photoconductivity dielectric layer on a target electrode, it is possible to make it increase by the exposure of light, and this is illustrated by drawing 4 B. The pattern of deposition follows the pattern of an exposure of light so that drawing 5 B may explain.
The other physical elements known as what changes the conductivity of the impregnation (1969 besides a raiser) of partial heating of a dielectric layer and a carrier which carried out the electric charge, an exposure, and a dielectric are also used in order to adjust deposition of electrostatic atomization like the case of a mask with a hole.
When approach a base, it is arranged, the thin conductive mask with which the same potential as a base was given is passed and deposition of electrostatic atomization is carried out, a deposit will follow the form of the hole on a mask correctly, and a sample molecule will be distributed on a deposit at homogeneity.
However, many molecules in a sample accumulate on a mask, and are lost. Therefore, the configuration of the electrostatic field of this electrostatic atomizing process is very inefficient-like, and consumes time amount.
However, when the same polar potential as the source of electrostatic atomization and a minute drop is given to this mask, the preferential deposition of the matter by which electrostatic atomization was carried out is performed very efficiently. The reason is because the orbit is changed so that that to which the electrified mask ****ed the matter by which electrostatic atomization was carried out, and electrostatic

atomization was carried out may pass the hole of a mask. The phenomenon relevant to the repulsion effectiveness of the electrified dielectric or the conductive electrified mask is distinguished here. The first phenomenon is called "electrostatic concentration" and this repels a charged particle in all the area of masks other than the location close to a hole, or the location close to the spot which has irradiated the light on the dielectric of a photoconductivity. Then, particles are collected by the electrostatic field which passes a hole as shown in drawing 3 . With the electrode 50 with which the forward potential set into the capillary tube 52 was given, the solution of the nonvolatile matter 54 by which electrostatic atomization is carried out from a capillary tube point will be in an unstable condition, and electrostatic atomization of this matter will be carried out like the shape of a torch 56 from a capillary tube tip. The orbit (an arrow head shows) of the particle which faces to a base 58 is bent, passes the hole 60 on the electrified mask 62, and is converged. It deposits on a film 64 in the configuration and magnitude equivalent to the hole of a mask. Only when an orbit as shown in drawing 3 A to all charged particles is made, such uniform deposition is attained. By the second phenomenon, when the spatial include angle at the time of a charged particle advancing into a hole becomes near perpendicularly as shown in drawing 4 (thing with the hole with which a large number approached) as shown in drawing 3 B (electrostatic atomization in the electrical potential difference in which the lowest electrostatic atomization is possible) or, the uneven electrostatic field near the spot which has irradiated a hole or light turns the orbit of a particle in the center of a hole, and is deflected. The redistribution of a deposit which can set this hole caudad is called "electrostatic concentration effect" or the "lens effectiveness." The matter with which electrostatic atomization of the case of the latter was carried out is deposited as a spot of size smaller than the hole on a mask. Not all the charges shown in drawing 3 A and drawing 3 B can affect the whole process, but it can use it as a reverse charge.

An operation of this electrostatic lens differs from the thing of an electron microscope notably. It is because the inertial force which determines an orbit can be disregarded in an electrostatic lens in a vacua since, as for the reason, viscous force excels in the atmospheric air of a steady state. By this electrostatic-lens effectiveness, there is an advantage that the size of a deposit is fairly smaller than the hole of a mask, and since this does not have to make a hole small to same extent as a spot, it decreases fairly the technical issue of the mask manufacture corresponding to deposition (spot) of a deposit smaller than a micron or a micron. The result of the electrostatic-lens effectiveness which used polypropylene textile fabrics as a mask is shown in drawing 5 A - 5B. A protein spot (drawing 5 B) with a fairly smaller than the 23-24-micron hole (drawing 5 A) which left only 47 microns mutually in the polypropylene textile fabrics used as a mask size of 5-7 microns is obtained. The advantage of electrostatic concentration is that the matter by which electrostatic atomization was carried out accumulates at about 100% of effectiveness, in order that the electrified molecule may not carry out little deer absorption of the mask very much. For the existence of the single hole on a mask, electrostatic concentration effect is in a repressed condition, and drawing 14 A and 14B show that a uniform deposit film can be manufactured.

The electrostatic-lens effectiveness is used, also in order to manufacture a sample with high exterior and height-horizontal ratio so that it may explain to an example 10, and the needlelike array of a RNAse sample is manufactured by this by using the mask shown by drawing 5 A. An organic substance [like light green coloring matter] whose array of such a rod-like sample is is also manufactured. even in (18% of humidity [An example 10]) the condition of it having been comparatively alike and having dried from these experiments, it can conclude that a protein film has sufficient conductivity to pass a charged particle through a film with a thickness of 40 microns or more. Impregnation of the high electric field and the high charged particle in deposition of electrostatic atomization causes [of such a protein deposit as well as the deposit of an organic substance] a conductive increment (1969 besides a raiser).

The mask used by this invention has the array of a single hole or a hole, and this mask is arranged between the source of electrostatic atomization (capillary tube), and an object. It is suitable for this mask that it is made of the non-conductive matter, on a master, when the first electric charge molecule by the electrostatic atomizing process adsorbs on a mask front face, electrostatic concentration effect is attained automatically, therefore adsorption of a subsequent charged particle is prevented electrostatic. The non-conductive part (area) of the mask which has the adsorption layer of an electric charge molecule makes the hole of a mask point to all the electric charge molecules by electrostatic atomization, and has the function of a up to [a base] made to deposit. The same electric concentration effect can be observed also when a dielectric photoconductivity layer is used as a base.

This mask can also be made from the conductive matter. However, since the potential of the conductive mask used by the approach of this invention makes it point to an electric charge molecule to a hole, it should adjust in the middle of the potential of the electrode on a capillary tube, and the potential on a base. By this,

the loss of the considerable amount of the matter by which electrostatic atomization was carried out can be prevented.
In electrostatic concentration, although the electrostatic-lens effectiveness occurred very easily with the mask with the array of the hole which approached mutually, it confirmed that it could be said that there is little electrostatic concentration or there is with two or more holes detached more greatly than the diameter of a single hole or a hole. [no] When arranging directly the plastics plate which opened the hole of a piece on a base, if the thickness of a plastics plate is increased 0.5 times of the diameter of a hole, the greatest electrostatic concentration effect will be obtained. However, in arranging above a base the thin mask which opened the same hole so that only the distance from a base to the surface upper part of a thick plate may estrange, extent of electrostatic concentration effect decreases and the configuration of a deposit becomes what deformed from the configuration of a hole. it is shown that the aerodynamic study-force caused more in the style of ion controls the process of electrostatic concentration only by electrostatic force 7s **s from these things. It also turns out that it is dependent on the location (the smallest spot will be obtained if a capillary tube approaches above a hole and is arranged) of the capillary tube to (as for the deposition in the minimum [applied voltage / to a capillary tube], concentration becoming large) with an electrical potential difference and the hole with which electrostatic concentration is impressed to a capillary tube.
Thus, in order to distribute the matter over homogeneity using the hole of the piece of the configuration of arbitration, it is suitable that the following conditions are fulfilled.
(i) A dielectric mask is thin.
(ii) A mask is arranged near the base.
(iii) The source of electrostatic atomization is not arranged right above the hole.
(iv) The surroundings of the vertical axes which pass a base and a mask through the center of the hole of a mask are rotated.
(v) A means to make the air of the neighborhood of a hole stir is established.
Under such conditions, the form and size of a deposit follow the form and size of a hole.
In order to carry out electrostatic concentration with each hole, a thick mask with the hole which carried out the trapezoid form is suitable.
If the particle from an electrode adsorbs on a mask front face when a mask 62 contains a dielectric, an insulator, and semi-conducting material, an electrostatic electric charge will occur. Although that which is separated electrically (or insulation) is suitable for a mask, making it grounding, in order to make the charge collected too much alternatively discharging a little slowly, or the electrostatic electrification equipment mentioned later can also be used for it.
Drawing 4 A illustrates the hole 60 of many masks like drawing 3 A and 3B. This equipment is the same as that of drawing 3 A by which the electrostatic atomizer containing a holder 50, and the electrode/capillary tube 52 which makes the fog of a charged particle 56 is illustrated, and 3B. However, the mask 62 named 62 by drawing 4 A is partially [metal or / at least] made of the conductive thing (for example, thing which made sandwich structure the matter with different conductivity, or the thing containing a semi-conductor), and it is suitable that it is a dielectric. Every charge moves in a front-face top (charge for example, on a mask 62), and it concentrates on a conductor at an angle or a point as electrostatics is sufficient and it is known at the case. If the hole is geometrically the same, the inclination of the surrounding potential of all holes should become the same.
Bases 58 may be a dielectric and a conductor or may have various conductivity. It is suitable for a base 58 to connect with electrostatic equipment 581, namely, electrification equipment, i.e., electrostatic potential induction equipment, and it may attach the electrical-potential-difference adjustment 582 alternatively. As for these, it is possible to also make it attached in the equipment of drawing 3 A and 3B (however, drawing 3 A and 3B do not show). This 1st electrostatic equipment is held to the 1st potential which draws a charged particle 56 for the up front face of the base 58 near the deposition part 64.
A mask 62 may be alternatively connected to the 2nd electrostatic equipment 621, although it can also insulate and it is possible to also make it dependent on absorption (or reduction) of a charge for [the] the optimal polarity. It is suitable to become independent of the thing to which the electrical-potential-difference adjustment 622 is attached, or a base 58. Without making it deposit on a mask 62, an electrical potential difference can be optimized in order to centralize a particle on the target deposition area 64. For example, it is suitable for a mask 62 to be maintained at the condition of opposing in potential to a charged particle 56. Thus, it can be made to act as a physical shelter and electrostatic field effect equipment.
The electrostatic equipments 581 and 621 can be equipped with a dc-battery, the current supply section, a Volta cell, etc. An adjustment 622 can be used as a certain hand control which adjusts the electrical potential

difference of a mask 62, or an automatic gear.
Drawing 4 B is other suitable examples, and makes the pattern of various charge concentration by use of light.
This mask 62 may be made of what was not only limited to a conductor and a dielectric, may be made of any matter, or contains special matter like a photoconductivity polymer and a semi-conductor. In drawing 4 B, shape is taken as an optical mask 162, and it is suitable for a mask 62 to be arranged under the upper twist straw-mat base of a base, and it is named 158 here. This mask projects a shadow on the base lower part. In this suitable example, a base 158 contains the layer of the layer of the thing of photoelectromotive-force structure which the matter with a photosensitive electrical property (suppose that this is called "electrosensitive [electrosensitive (electrophotic)]" on these specifications), for example, a semi-conductor, and light are answered [thing], and makes a front face produce an electrical potential difference, photosensitive polymer, or other matter. A base 158 is equipped with the sandwich structure containing the layer of the transparent conductive plate which functions as an electrode, and a photoconductivity in this suitable example.
The simplest structure of a layer 158 is the aperture plate of the opaque matter which equips the bottom of the deposition part 64 with a hole 160. It is suitable for the light source 170 of a lamp, laser, and others to irradiate the light collimated through the hole 160 so that it may mention later, and to form the deposit of a charged particle 56.
Or instead of using a mask 162, a desired beam-of-light pattern can carry out the trigger of a modulation scan laser beam, a phot cel, or the laser array alternatively, or can also make it from this invention by the thing equivalent to these.
Drawing 4 C is the sectional view of the transverse plane of the base 158 in drawing 4 B. It is suitable that a base 158 contains the transparent conductive layer 1582 and a photosensitive layer 1583 like photosensitive polymer in order including the transparent physical supporters 1581 who consist of plates, such as glass and a product made from an acrylic, from the bottom. For example, a transparent conductive layer shall contain a metal film partially on the transparent conductive matter or a base 1581.
A typical photoconductivity polymer film serves as conductivity with light, and if there is no light, it will serve as insulation. Therefore, the part of the layer 1583 which the mask 160 was passed and was irradiated from the bottom serves as the same potential as a conductive plate. It is because the electrostatic charge with the superfluous reason is discharged through the conductive layer 1582. It is suitable for a layer 1582 to connect with the electrostatic equipment 95 to which the electrical-potential-difference adjustment of an option was attached. Moreover, a layer 1582 can also be grounded simply.
The part of the layer 1583 which was not irradiated between them will reach the potential which changes with absorption, or will only hold former potential with non-conductivity. This particle will be deposited only on the deposition area 64 on the hole 160 in an optical mask 162, in order for the particle 56 of a spraying object to be repelled by this different potential and to draw depending on the potential of the irradiated part.
Drawing 5 D shows the result attained by the electric exposing method of this invention.
The pattern of an exposure can be used as the negative of a photograph and the same result can be obtained by making the polarity from equipment 95 opposite in this case (not shown in drawing). The means of a certain other electric exposing methods for making the potential for generating a deposit 64 is also included in the range of this invention.
When electrostatic atomization is carried out, in order to hold the structural and functional property of protein and biomolecule like DNA, the electric-field field strength in the capillary tube tip of the source of electrostatic atomization must not be as high as corona discharge breaks out, although it should make sufficient reinforcement for electrostatic atomization to function. Corona discharge is because the functional property of biomolecule is destroyed. The electric-field field strength in the capillary tube tip of the source of electrostatic atomization can be adjusted constant current and by reaching or maintaining a constant voltage. The minimum electrical potential difference and the minimum current are determined by experiment. It became clear that it depended on the distance between the radius of a capillary tube, the conductivity of a solution, a flow rate, and a capillary tube-base for the minimum electrical potential difference which confirms electrostatic atomization. Distance between about 20 - 30 microns and a capillary tube-base is set to about 15 to 40 mm for the diameter of a capillary tube, and electrostatic atomization of the protein solution is carried out very effectively in current abbreviation 10-50nA which reaches an electrical potential difference by three to 5 kV, and reaches a flow rate by part for 1microl./. If a current exceeds [an electrical potential difference] 100nA(s) by 6kV or more, the property of biomolecule will be

easy to be destroyed in the process of electrostatic atomization. If air is permuted by chlorofluocarbon, carbon dioxide gas, and the gas that controls other corona discharge, it will be helpful for preventing corona discharge. If electrostatic atomization is assisted according to gas-jet spraying, since the drop of micron size will be obtained on an electrical potential difference fairly lower than the electrical potential difference needed only by electrostatic atomization, corona discharge can be controlled. Since the electrostatic atomization assisted with jet can acquire the distribution stabilized by only electrostatic atomization also by the more fairly quick flow rate, it promotes deposition of the matter powerfully. Air-bleed assistance can make a big sample and a lot of samples deposit effectively especially like the electrostatic atomization of ultrasonic assistance (a thing like the ultrasonic spraying instrument of ANARITIKA in Bradford). It is because it can be made to distribute easily until the flow rate of a solution results in 1 mL/min.
In order to make coincidence carry out the electrostatic atomization deposition of two or more spots from a single capillary tube through the mask which has the array of a hole, it is suitable to vibrate the capillary tube on a mask. Moreover, it is suitable for the base/base material for an electrostatic deposit to make it rotate. It is for making homogeneity deposit the particle by which electrostatic atomization was carried out in the place which each spot reaches. Also when moving a capillary tube and a base relatively in other modes under the conditions which make the same assembly time in the deposition location on a base, deposition serves as homogeneity. And it can opt for the migration by this contractor. Other methods of making homogeneity deposit the electrostatic atomization matter are installing a capillary tube in the protective plate / electric shielding plate which the hole's opened so that it might explain below. It is suitable for a capillary tube to be made to stand it still, if it is made when uniform thickness deposits one sample (for example, rectangular protein fragment), although it has a complicated configuration, and not to make it located right above the hole of the non-round shape prepared in the mask, but to rotate a mask, and a base/base material. Thus, if a mask, and a base/base material are rotated, a charged particle comes to approach a hole from every direction at homogeneity, and can avoid the electrostatic concentration effect of a hole. The protect ring with which the potential of the sign same generally as the electrification charge of a minute drop which separates from a capillary tube tip was impressed is arranged on the almost same level as the level at the tip of a capillary tube, the minute drop charged in the location where electrostatic atomization discharge takes place is repelled, and it is made to surround with a charge which prevents dispersion in electrostatic atomization. A protect ring is not limited only to such an example, although it turns out that it is transposed to a plastics electric shielding plate like two examples shown in diagram in drawing 16 A and 16B, and an effectiveness target. These plastics electric shielding plates can also be used as a trapezoid or a cylindrical shape. A wall is charged and dispersion beyond it is made to prevent by deposition in the wall of some such shelters of the matter by which electrostatic atomization was carried out. Similarly, it also became clear that the wall of such a plastics shelter could be made from the plastics textile fabrics which make air penetrate.
There are three advantages in the design of this latter.
(i) So that a lot of charged particles may be shut up and carried out and drawing 16 C may explain together with mutual repulsion of a charge, when surrounded by the drying [easily]-from matter by which electrostatic atomization was carried out-solvent (ii) shelter a trapezoid grid which was illustrated by bringing-result to which location limited with such electric shielding plate is made to carry out uniform deposition (iii) drawing 16 A makes concentration of the flow of a particle easy (this is important in especially deposition of a minute sample) -- it comes out.
It depends on the property as a dielectric (it is required that the conductivity of bulk and a front face should be low) of the matter of a shelter and a mask, the distance between tip-bases, and the whole surface product of a hole for the effectiveness of the deposition in the approach mentioned above. In two or more holes which are explained by drawing 5 A, or the single circular hole of a 1.5 to 5 mm diameter, effectiveness 70-80% can be obtained easily.
When a hole is made to reduce to 2 by 0.2x0.7mm, effectiveness will decrease to 4-10% as a result. It became clear that installation of the additional convergence ring (two to 5 mm diameter) installed in the same axle in the horizontal plane of a plastics mask carried out the considerable increment of the effectiveness in the potential adjusted proper on a convergence ring. In order to adjust potential, it is necessary to measure to coincidence all the currents that pass a capillary tube as well as the current which passes a sample.
In future explanation, electropositive potential is impressed to a capillary tube and it is assumed that it is that to which the sample holder is grounded. If the increment in specimen current will be observed, the potential of a ring will increase further, if the potential of a convergence ring is made to increase (it is from zero in

the condition of being grounded), and a current passes maximum, a current will decrease after that until generating of electrostatic atomization is inhibited completely. The fall of all currents which passes the capillary tube by the increment in ring potential is accompanied by the reinforcement of the thing of the shape of a torch by which electrostatic atomization is carried out becoming weaker. It became clear that the deposition in the electrostatic atomizing process under the conditions that the currents which pass a sample holder are 50-90% of all currents passed one hole in the mask of the hole below millimeter size, and protein was made to deposit at 20-40% of effectiveness as a result. It is very efficient to make many minute samples deposit on coincidence, and a convergence ring is not usually needed. However, the dielectric mask which has two or more holes can also be covered in the convergence network of two or more rings so that each hole may become in the center of a ring, and all rings can be connected to the current supply section with an electrical-potential-difference accommodation machine like the collector in the single hole mentioned above.

The other potential problems in the case of passing and depositing the small hole of a dielectric mask are that deposition of the matter directly sprayed on the dielectric mask near the hole decreases the whole effectiveness fairly. Extent of deposition in up to such a mask front face changes depending on existence of the conditions of the class and others of the polymer used, for example, an electrical potential difference, the charge of the sprayed particle, and a convergence ring, and a diameter. Especially, in this invention person's laboratory, when the mica was used as mask matter, it became clear that deposition of a up to [a mask front face] decreased. Probably, such mobility can also be made high although it is a reason that the mobility of a mica of the poured-in charge is more low or that there are more few electron holes compared with plastics (1969 besides a raiser).

It is suitable for the base or base material which a charged particle deposits to have high conductivity. However, a thing (semi-conductor), has the low other matter, i.e., whole conductivity, or what has surface low conductivity can be similarly used as a base. As for the example of such matter, paper, hydrophilic plastics, a membrane filter (for example, the IMMOBILON-P filter made from PVDF, a nitrocellulose filter), a mica, and glass are contained. Although a mica and glass do not have conductivity in the condition of having dried, in the wet condition or the damp air, conductivity is shown in a front face. The filter also has conductivity similarly sufficient in the high (70% or more) or air of moderate humidity (30-50%) to use as a base.

With an example of the suitable example of this invention, the deposition by the electrostatic atomizing process to what does not have conductivity in a front face is attained like the dry mica, glass, and dry plastics by performing regrouting of a periodic charge to a front face without conductivity by the ionic current of the reversed polarity from corona discharge so that it may illustrate by drawing 34 . The ionic current of reversed polarity is generated according to the array of the electrode in the covered chamber. Regrouting of such a charge has the advantage that the continuation layer of a charged particle deposits on a base, by repeating the cycle of spraying and charge regrouting. If this advantage does not exist, the electric charge molecule piled up on the base will inhibit the deposition after it. In the example of the front face of a mica, it is covered with a mica sheet on the rotating disk made from plastics, and it is regrouted in a charge by passing directly under a micro electrode with the period of the rotation. a mica -- being related -- a capillary tube -- forward and negative -- both of the electrical potential differences can be applied. In order to decrease surface conductivity in the mica of this example, while making it deposit, it is necessary to dry a mica front face with heating using the source of infrared radiation, or the dry warm air. Deposition is possible for example, among atmospheric air also within the chamber which had the ambient atmosphere adjusted.

It is desirable to exfoliate considering the quality of a deposit as a sample film from a base or a base material under a certain situation. In order to help this exfoliation, an interlayer can be prepared between sample-bases. Thus, a sample film can be moved to measuring equipment. After the biomolecule which needed to have conductivity and was deposited by electrostatic atomization carries out the crosslinking bond of a part of this interlayer, he must be an easily removable thing. as the example of the matter which can be used as an interlayer -- the following -- it is .

(1) Existence of water, the polyacrylamide which reaches, or sets under other conditions (i.e., change of pH), and is swollen and dissolved slowly, or a water-soluble polymer layer like a polyethylene glycol.

(2) The layer of the polymer which has association of the disulfide which can be disassembled (chemical decomposition) when a mercaptoethanol solution is contacted and which is marketed. Therefore, a polymer is decomposed as a result.

(3) The layer of the carbon distributed by the altitude which has low adhesive strength in the deposited

biomolecule.
(4) It is the layer of the carbon system polymer which is a conductive compound, and other low-melt point point conductive polymers. Drawing 6 illustrates the suitable example of the manufacture process of the sample film on an interlayer, and the process of the exfoliation from an interlayer. The auxiliary layer 80 of half-conductivity as an interlayer is first deposited on the layer 81 of the conductive base on a base 82 using electrostatic atomization or other known approaches from a capillary tube 84. And the hole [in / for the sample film 86 of desired biomolecule / a mask 90] 88 is made to pass and deposit after that using an electrostatic atomizing process. By dissolving the auxiliary layer of half-conductivity using a solvent 96, a sample film exfoliates from a base and can be attached in the point of measuring equipment 94. Or it can also consider as the sample which exfoliated by lifting a film from a base simply. The suitable example of the interlayer as exfoliation of a sample film is the auxiliary layer of an alginic acid, and although an alginic acid is insolubility by acid pH at a solution, it can be easily dissolved in a solution by alkaline pH.
In deposition of an electrostatic atomizing process, when protein is used as an example of biomolecule, it depends for the structure of a protein film, and the functional property of the protein molecule on a film on existence of temperature and humidity in case electrostatic atomization of the flight stroke of electrostatic atomization, the rate of the charged particle adjusted with an electrical potential difference, the sign of a charge, and the protein molecule is carried out, the protein concentration of a solution, and a stabilizer. The minute drop by which between short distance, for example, a base-capillary tube, was among (70 to 80% or more of relative humidity) the atmospheric air with which about 15mm or electrostatic atomization became wet, namely, electrostatic atomization was carried out when carried out by the wet electrostatic atomizing process and which carried out the electric charge arrives at a front face without not decreasing or generating desiccation ion. The sample film obtained after drying the minute drop deposited on the base has the common feature of the sample obtained by the conventional method of making a protein solution apply to a direct base, and drying protein, and many. In the mechanization study-reaction to ligand like calcium2+, the difference which was conspicuous with the film of alpha-lactalbumin generated by deposition of the wet electrostatic atomizing process to the glass front-face top covered by conductive SnO two-layer and the film of the same enzyme generated by the conventional method is not detected.
The deposition by the electrostatic atomizing process of biomolecule can also be used as a means of minute amount concentration of a thin biomolecule solution. By changing the conditions (flow of the gas dried the humidity of 40 to 50% or less, and the distance of 30mm or more between capillary tube-bases) of electrostatic atomization, the ion of the nano cluster and biomolecule which deposition was performed by the drying method in the condition that concentration of the biomolecule in a minute drop occurs, and were dried is deposited on a base. It became clear with the force tunneling microscope between scanning atoms to deposit huge biomolecule in the state of the dry single molecule, if the solution concentration is merely about 10-3-10 to 5 mg/less than ml of a critical value. The nano cluster which is what has a large number by the dry type approach in high concentration from this at an electrostatic atomizing process forms the film of opaque porosity so that it may illustrate by drawing 15 A.
The protein molecule of the film manufactured by the dry type electrostatic atomizing process holds the functional activity. The minute data by which the data hung up over Table 1 consist of various protein manufactured by the electrostatic atomizing process point to showing the mechanization study-reaction of the same level in specific ligand to the film of such protein manufactured by the conventional dry type approach. Maintenance of the functional property of others about the protein molecule in deposition of electrostatic atomization is explained by the example 3. Similarly, drawing 12 A, and 12B and 18 explain the activity of the peroxidase of a horseradish, and the enzyme of alkaline phosphatase.
An example 4 explains the maintenance of the property as a proteinic antigen by which electrostatic atomization was carried out.
Table It is a pair to the specific ligand about the film of the protein of the versatility manufactured by 1 electrostatic atomizing process and the conventional method (what dried the protein solution on the glass front face) by which the crosslinking bond was carried out. Comparison of the mechanization study-effectiveness to carry out

蛋白質	リガンド[1]	乾式試料の効果[2] %	静電噴霧法における堆積物資料の効果[2] %
膵臓 トリプシン	プロフラビン 塩基	+69 +23	+72；+72 +37；+38
アビジン	ビオチン	-51	-41；-48
シトクローム－C （馬）	亜ジチオン酸塩の還元物	-30；-50	-41；-49
リゾチーム （卵）	N-アセチル- D-グルコサミン	-7.7；-8.7	-6.3；-3.5
ヘキソキナーゼ （イースト菌）	グルコース	+31；+38；+44	+44
アルコール デヒドロゲナーゼ （馬の肝臓）	NAD	＋3.5；+6.2	+2.7；+7.4
α－ラクト アルブミン	Ca^{+2}	+240	+370
コンカナバリン A	Ca^{+2} , Mn^{+2} α-D- mannopyranoside	+10 +11	+6 +4
膵臓 RNAse	3'-シチジン 一リン酸	+4.0	-3.4
3-ホスホグリセリン酸キナーゼ （イースト菌）	Mg-ATP	+13	+16

1 The ligand concentration in each test surpasses five to 10 times of a known coupling constant.
2 Express relative change of the isometric tension in the protein film in which induction is carried out by association of each ligand. Although the highest conditions for making protein deposit changed with each protein, it became clear that the result it should be satisfied with almost all water-soluble protein of a result in the following conditions was obtained. They are the conditions of 10-15% of glycerol, and beta-mercaptoethanol of 100-20mM to one to 10 mg/ml protein concentration, sugar or trehalose 25-40% (desiccation protein, w/w), and desiccation protein. The conductivity of the protein solution manufactured for electrostatic atomizing processes should not exceed cm in 500micro siemens /. Otherwise, it is because advance of deposition becomes very slow and the capillary tube tip of micron size is needed. Usually, adjustment of pH is not required unless the stability of a protein molecule is spoiled. Before spraying, beta-mercaptoethanol should be added quickly. The following spraying conditions are [for manufacturing the single protein minute sample for a mechanization study-trial] standard. Height from relative humidity 10-40% and a sample holder to a capillary tube tip; ten to 14 mm, a +two to 3 kV capillary tube electrical potential difference, ring electrical-potential-difference +(0.5-1.5) kV of a collimator, a total of five to 10 nA of a current, current 3-7nA that flows a sample, a protein film with a single thickness of 1 - 2 microns (0.2x0.2mm wide)
Although the sum total of assembly time which can be boiled and set takes 3 to 15 minutes, this is dependent on protein concentration.
It is considered to be the most important of all parameters to maintain low the total current which flows a capillary tube. If a current is set to 10 to 100 or more nAs so that drawing 18 A and 18B may explain, the

specific activity (specific activity) of alkaline phosphatase will be checked notably. Low current is effective from a viewpoint of effectiveness similarly. The electrified cluster is repelled from a hole with the superfluous space charge formed in the surroundings of the hole of a shelter, and the amount of the electrification cluster deposited on a collimator and an electric shielding plate is made to increase under a high current.
Since the conditions which manufacture the sample which consists of two or more components by the electrostatic atomizing process are performed with the high current which is a high flow rate so that there may be no loss efficiently, they differ from the above remarkably. The conditions of others which can make deposition of a substrate change greatly are a solvent (for example, if glycerol 10-30% is added to protein or a DNA solution, the distance between base-capillary tubes will be long, and will enable wet deposition on a porosity filter even in low humidity), concentration, temperature, humidity, and a base.
furthermore, the thing for which it helps quick desiccation protects protein from damage rather than being attained by dry type electrostatic atomization, and a protection reagent like trehalose, cane sugar, other carbohydrates, and other polyols is added -- damage -- and -- or deactivation by desiccation is protected.
When carrying out electrostatic atomization on the quiet conditions of a low battery, low current, and the adjusted humidity, existence of cane sugar protects the activity of AP from the same solution used for electrostatic atomization compared with the case where direct drying of the alkaline phosphatase (AP) is carried out, on the same base. It became clear that the specific activity of AP enzyme deposited by electrostatic atomization under ****** conditions is comparable as an early enzyme solution. In order to inhibit damage by the radical generated in process of electrostatic atomization, active oxygen, and chemical species [activity / others], a radical scavenger and an antioxidant can be added as a protection reagent. For the protein which has an important isolation sulfhydryl group atomic group to a functional property which exists in hexokinase Existence of beta-mercaptoethanol which decreases the drugs which make the oxidation of the sulfhydryl group atomic group of a solution by which electrostatic atomization is carried out inhibit
As long as it judged from the rise of the mechanization study-reaction in association of the specific ligand of a protein film by which electrostatic atomization deposition was carried out, it became clear that it resulted in making a functional property hold well fairly. beta-mercaptoethanol can be similarly committed as a radical scavenger and an antioxidant. Thus, it is effective also to protein without a sulfhydryl group atomic group to add these drugs.
Furthermore, in the approach of this invention, carbohydrates, such as a glycerol, cane sugar, and trehalose, and a protection reagent like polyol can also do the thing of the sample film which was deposited during desiccation in addition to protecting biomolecule from damage also for which the pack density of biomolecule is decreased especially in protein. The additives of these protection reagents are water solubility and a non-volatile. After the crosslinking bond of the dry biomolecule is carried out, a water-soluble non-volatile additive is flushed, therefore an additional hole and an additional channel are made in a sample. Thus, the pack density of the sample film by which the crosslinking bond was carried out decreases, and the permeability to the sample film of ligand improves. Such a film is more efficient in the test using the specific ligand of bigger molecular weight and bigger size.
The approach of others which raise the permeability in reduction of pack density and the sample film of biomolecule is used by the dry type electrostatic atomizing process in a high-concentration biomolecule solution, and biomolecule deposits it with the gestalt of a minute cluster as a result. It depends for the size of the deposited minute cluster to biomolecule and its solute concentration strongly. As drawing 15 C explained, the internal diffusion in the film which consists of a minute cluster deposited by the electrostatic atomizing process becomes very quick rather than the film by the dry process of the same protein. The reason is that ligand permeates the channel between big particles easily, and the diffusion rate of a between [particles] becomes slow to the same level as the case of a homogeneous film.
As explained in the top, although it is thought that big ligand tends to permeate a sample film with low pack density, it is considered to be a main method of decreasing the diffusion limitation in a sample film to make thickness of the deposited biomolecule layer thin. It is thought that the monolayer of the biomolecule which accumulated on the suitable matter or became independent is the limitation of a thin film completely free from any internal diffusion limitations. In order to use for a mechanical test, the crosslinking bond of such a film is carried out internally, and it can be made to deposit on the front face of the gel which is independent, and is made to exist or does not restrict migration of a monolayer film. In other analysis (for example, used by the plasma resonance sensor, an immunoassay test, etc.), although a monolayer film or the molecule divided into homogeneity can be made to deposit by the electrostatic atomizing process on the suitable matter within the limits of the conventional technique, it is not necessary to carry out the crosslinking bond,

either.
The drugs for making the crosslinking bond of biomolecule possible may be set to the advanced technology, and are known (1991 besides Hermann Son). The exposure of ultraviolet rays is used to a DNA molecule. Since there is an advantage to a protein molecule about the maintenance of proteinic functional activity by which the crosslinking bond was carried out, glutaraldehyde is suitable. Glutaraldehyde attacks the isolation amino atomic group which exist in a protein molecule, and unless, as for the conversion object, the amino-group atomic group is contained in the direct active site, there is no auxiliary operation over a proteinic functional property. Reversible maleylation [in / in the amino-group atomic group on an active site / alkalinity] (maleilation), Although protected from a reaction with glutaraldehyde by deblocking (deblocking) by the alkaline crosslinking bond and are recording [in / a little / acidity (pH 5-6)] (storage) etc. In protein which, on the other hand, has an amino-group primitive team all over an active site at this invention person's laboratory, such as an antibody of RNase and single clone nature Even when the amino-group group was not protected, it checked that ligand association could still detect as checked by affinity analysis on this film. However, in order to obtain a bigger SN ratio, taking care of an amino-group primitive team has it, when protein has many isolation amino-group primitive teams or the amino-group primitive team of a binding site. [effective]
the air or the solution (for example, it is for giving migratory and the fluidity which were limited to the biomolecule in a glycerol solution and a sample film, and is not for giving fusibility to a solution) which became wet about the film of biomolecule in specific protein before the deposited biomolecule carried out the crosslinking bond -- also putting -- it is good. the effectiveness of a fluid rise -- the protein molecule of a film -- and -- or a cluster can be moved mutually, the hole in a film can be buried, and the heterogeneity of the appearance of a film can be abolished. This phenomenon can be connected to the deterioration in the layer of the round big stone irregularly planted by the front face. If a big stone becomes movable relatively by a certain disturbance, a big stone will move so that it may become homogeneity more structurally. However, reinforcement can be enlarged although reduction of ligand penetrating power is sacrificed for a proteinic uniform film.
As compared with the conventional approach of forming two or more deposition spots, the approach by this invention has the following advantages.
How (the manufacturing method of the Stanford University DNA library is resembled.) to use the approach on which the spot of the matter is made to put directly manually, or the manipulator by which computer control was carried out 1996 besides Sharon are referred to -- **** -- if it compares -- (i) -- a considerable small spot can be made to deposit
(ii) Since two or more spots can be deposited on coincidence, production time can be shortened notably.
(iii) A spot is made to any forms.
(iv) Since it is condensed as a surface layer, without covering the whole thickness of a membrane and distributing the matter when making it deposit on a filter membrane, it becomes easy to find a spot by the optical approach.
As compared with the approach of using the electrodeposition from a solution, the deposition by the electrostatic atomizing process is advantageous in respect of the following.
(i) A micro electrode array is not needed for deposition of a minute sample.
(ii) It is value ****, using as a base material the front face which has conductivity level and slightly. For example, the mica in the damp air and the front face of glass have sufficient conductivity for making the matter deposit on it. Drawing 5 C shows the example of the deposition approach of a up to [the damp mica front face by the electrostatic atomizing process which passes the electric shielding plate shown in drawing 5 A].
(iii) When the contamination between spots of the various matter which may be produced when contacting a solution deposits various matter continuously, it does not take place.
Compared with the photograph RISOGURAFU method, the deposition by the electrostatic atomizing process has the following advantages.
(i) The routing counter in a deposition process should decrease.
(ii) Since the number of the chip which moves through an interface with a solution decreases since the whole chip front face is non-contact [each / solution and non-contact] when dipping in a decreasing [cross contamination] (iii) solution, or when pulling out from a solution, cross contamination should decrease.
There is an advantage of the following propers in the deposition technique by the electrostatic atomizing process.
(i) In a conventional method, the deposition of electrostatic atomization is possible under the conditions

which were not able to be attained. For example, the matter can be deposited on the front face extremely cooled by low temperature. That is, it can deposit under existence of liquid nitrogen or a dielectric fluid so that drawing 7 may explain. Such a low temperature service may be effective in deposition of an unstable molecule. The deposition under a vacuum is possible for the deposition by the electrostatic atomizing process similarly. By the approach same with pouring in ion by the mass spectrometry, the electrified molecular cluster can be poured in under a vacuum.
Or by arranging a base behind the input port of a mass spectrometer, it dissociates before deposition and the component from which the solution by which electrostatic atomization was carried out was separated deposits the matter on the various locations of a base again. Thereby, a deposit can be further used now for a chemical analysis.
(ii) The internal structure of the matter deposited in electrostatic atomization shall differ from the usual thing. For example, the amorphous protein film obtained by the electrostatic atomizing process is not compressed with high density like the film obtained by drying the protein solution on a front face, but has that it is not homogeneous, either. Instead, the porous matter made from a protein cluster is obtained by the deposition by the electrostatic atomizing process of a protein concentrate solution as shown in drawing 15 A. Since osmosis of the matter into such a film becomes easy, such a porosity film serves as an advantage in an analytic application.
(iii) Since all the matter by which electrostatic atomization was carried out essentially faces to a base, the amount of substance to deposit can be adjusted easily. In the case of deposition of the biomolecule from the solution with which the joint effectiveness on the front face of activation of a different molecule differs, such effectiveness is not acquired.
(iv) In practice, since all the molecules by which electrostatic atomization was carried out pass the hole on a mask and reach on a base front face, they are very economical. [of the deposition by the electrostatic atomizing process]
(v) The deposition by electrostatic atomization is very flexible about the magnitude of a deposit. It is possible to apply the same technique to the spot of not only a small spot but the magnitude beyond 1cm or it like 1 micron.
The approach by this invention is used in order to manufacture the induction component of a biosensor from very a small amount of protein (0.01 to 1 microgram). This is important especially when testing the living body property of a protein molecule by the mechanization study-approach by change of the property of a protein film. The reason is because the protein of a microgram unit can usually be easily got by protein purification on a general analysis scale like electrophoresis. This approach can also be used in order to manufacture a protein sample for the biosensor which puts a foundation on change of the mass of the biosensor of other types, for example, an enzyme electrode, an MOSFET chemistry sensor, and protein, or an optical property. The approach of this invention which a micro sample generally manufactures from a molecule with a living body property offers the new approach of combining the living body property of the biomolecule in a nature, and signal-processing capacity and the integrated newest small chip.
Such an example of manufacture of a sample film is explained by drawing 6 , in order that the deposition by the electrostatic atomizing process may obtain the single sample film of the fixed protein, it is used, and this film is used for mechanization study-inspection of proteinic biocompatibility. The approach by this invention enables manufacture of a protein sample from the protein below the microgram which melted into the water of the number microliter. In order to carry out exfoliation of a sample easily, it is making a base with conductivity deposit an auxiliary layer beforehand, as shown in drawing 6 .
Plasma resonance (namely, commercially available ellipse reflecting microscope) and a scanning probe microscope (to one usable in order that a force microscope may discover association of the ligand to the array of the big protein molecule on a base front face, a tunneling microscope can be used in order to detect association of the DNA probe to the prehension-oligonucleotide which exists in the substrate on a base front face) are contained in the direct coupling detecting method which uses a sample film deposit.
The approach by this invention offers the approach of decreasing the magnitude of a required sample remarkably like sample manufacture of two or more components in all these approaches. For example, a scanning probe microscope can be used as an approach for discovering the interaction of the specimen in the molecule of others which were deposited in the shape of a matrix on protein or a base front face.
One of such the approaches is shown in drawing 8 . A scanning force microscope (SFM) / atomic force microscope (AFM) can measure the elasticity and the height of each spot of a matrix. Therefore, in analysis of a big specimen (namely, protein, a DNA molecule), in order that SFM/AFM may discover association of a direct specimen by the increment in the thickness of a protein monolayer like plasma resonance and the

mass changing method, it is used. The mechanization study-effectiveness in a protein deposit can also be used by the small specimen. Each spot (deposit) of a matrix increases by contact to specimen solution, and the elastic modulus changes so that the part on the right-hand side of drawing 8 may explain. The response of various components with various properties can analyze the solution which consists of two or more complicated components.
In order to carry out extensive manufacture of what acted to the shape of a matrix as TAISEI of the various matter according to the predetermined pattern to up to the base, after depositing each matter, it is attained when only a predetermined distance moves the dielectric mask or optical mask which has two or more holes. It is suitable for this migration length that it is smaller than spacing of the hole of an electric shielding plate. Thus, the pattern of a spot can be formed as a matrix array of two or more components. After a different solution accumulates respectively so that one spot in the matrix of two or more components can manufacture to coincidence under each hole in a mask as shown in drawing 9 , a mask or a base is moved by XY scanner. Although E is shown in drawing 9 from the solution A into which it was put by the separate capillary tube since it deposits as a different spot, on the other hand, the sample of many single components can also be manufactured very much to coincidence using the same equipment. For example, the hole of a mask is passed by this approach and the pattern of 200000 spots can be deposited on the area of a standard postage stamp size (about 2cmx 2cm) by electrostatic concentration of an electrostatic atomizing process. Drawing 32 and 33 explain two kinds of equipments for moving a base and a mask relatively. At drawing 32 , a movable stage is equipped with a mask and the plate of a lot with each movable within a slide is equipped with a mask by drawing 33 .
Thus, the approach by this invention offers making coincidence manufacture thousands of protein for using it for chemistry inspection, without using the matter with very difficult high price or acquisition, and a DNA sample. It is because each spot (deposit) by which electrostatic atomization was carried out can be manufactured from the matter of an about [10-7-10-17g] slight amount. An electrostatic atomizing process can also change the existing immunoenzyme technique into microscale similarly. For example, Antigen x can be distributed as thousands or more spots on a base with the powerful combining ability of covalent bond and others. After washing out an excessive antigen, each spot can be used in order to discover existence of the antibody to the antigen X in a blood serum. The united antibody is directly [indirectly or] detectable as an antibody of marker enzyme. The direct method which can detect change of the amount of the protein matter in a part of a spot like a scanning force microscope and plasma resonance can also be used. When the united antibody is detected indirectly, in a coloration enzyme reaction, insoluble chemical photogene and an insoluble fluorescent material can also be used effectively. If only 104-105 have an antibody molecule in each spot in a spot with a magnitude of 10x10 microns in easy trial calculation, it is measurable at an optical microscope. Thus, the induction component of 108-109 can make from the antibody which is 1 microgram. The advantage of others of this approach is promotion of an analysis rate. It is because the non-stirring layer made to the surroundings of a small body compared with a large body becomes much more thin, so the diffusion limitations in the case of association and washing decrease in number remarkably in a small sample.
Moreover, this approach can be used, in order to manufacture the matrix of two or more components, i.e., the various protein spatially distributed on a base, DNA, and other molecules, and in order to detect association in the array in the various antigens patternized on the base. The spot array of various protein can analyze two or more components in complicated mixture, such as a biological liquid and a natural extract. It is well known for the chemical analysis that it will decrease a property and the need for stability remarkably that the various sensors about various properties can be reacted to coincidence.
Manufactures of minute two or more analysis tests for immunity analysis are other examples which change the approach of being existing and use an electrostatic atomizing process. By the newest approach, the sandwich structure of the antibody which was visualized by coloring of the fluorescent material by the enzyme reaction and photogene, and was able to attach the antigen-antibody-indicator on the pint bottle of plastics is observed. The small amelioration version of ELISA by this invention has the array of the various antigens arranged on a base. The location of the base decides on the characteristic location of each antigen. When the antibody to the 2nd antigen exists as a solution, an indicator can be attached by the antibody by which the conjugated bond was carried out to the enzyme, and after adding an enzyme to a base, it is visualized easily, and each component of a matrix serves as insoluble coloring or a product of fluorescence as a result. By using the matrix of such two or more antigens, the antibody of a large number in a living body solution can be checked to coincidence by one analysis, and screening for inspecting a patient's immunity over a lot of checks, microorganisms, virus infectivity matter, etc. of allergen can be performed.

In the application of further others, the sample for making coincidence compound-ize two or more DNA probes (hybridization) can be manufactured using the approach by this invention.
The matrix of the spot which consists of various oligonucleotides and a fragment of DNA can also be manufactured on glass, a filter, and other suitable front faces, and can be used by conventional approach (1987 besides HAMESU) like the identification as a routine work of a living body kind, the immunologic tolerance of an organ, genetic analysis, and application of others of a dot blot (dotblot) technique. The molecule of lambda-DNA by which electrostatic atomization was carried out on glass or a nylon filter just attaches for it and mentioned above holding lambda-DNA probe by which biotin labeling was carried out, and the compound-ized capacity in the examples 7 and 8.
the same -- the sample of two or more components -- the approach of this invention -- the biochemical character of the matter -- it is manufactured for quick screening of the matter to kick. For example, a different organism or biological mixture is arranged at two-dimensional array. Then, the done matrix is contacted on the front face of a cell culture radical or bacteria culture-medium gel, and these matter is made to permeate into a matrix. At the reaction of the cell in a bacteria culture medium, some change, i.e., morphological transformation, a growth inhibition zone, etc. are observed. For example, the matrix containing the antibiotic known well is used in order to inspect the induction to the various antibodies of an infectivity microorganism so that the most effective art can be chosen. Similarly, since enzyme inhibitor is quickly specified from various matrix components, the approach by this invention is used. After contacting a matrix in the filter containing the saturated enzyme, enzyme inhibition can be found using a histochemistry reaction (histochemical reaction) so that it may continue all over the surface of action of a matrix and a saturation enzyme filter and enzyme activity may be distributed. For example, mass production method of the matrix containing the spot of commercial drugs offers an approach convenient to confirm the possibility of an auxiliary operation of these drugs by inspecting the reaction of drugs and much key enzyme.
The approach by this invention is applicable to manufacture of the pair NETO real library (combinatorial libraries) which is the field which is capturing the spotlight very much with sufficient convenience now. Since the compound of a two-dimensional library is discriminable on other techniques and contrast targets which design a pair NETO library with the location of an array, they do not take attaching an indicator to it. Manufacture of such a library that uses the deposition technique of an electrostatic atomizing process includes surface-activity-izing which can perform association (covalent bond) with a as strong front face as the specific components (N- or C-end polypeptide) of the structure of a compound, deactivation of all the nucleotides by which electrostatic atomization is carried out or amino acid, and a front face, the washout of excessive uncombined mixture, and activation of the end group group in an oligonucleotide or a peptide. As for such a series of steps, only the number with which the residue of a nucleotide or amino acid is introduced into a chain is repeated repeatedly.
As compared with the case where such a matrix is manufactured using the known technique which can be used with the conventional technique, the deposition by the electrostatic atomizing process by the approach of this invention can simplify a process very much, and can shorten process time amount. For example, a series of six masks both indicated to be also law to drawing 10 A-10F can be used, and a nucleotide can be continuously deposited on the library of 16384 components including all the possibility about the combination of the nucleotide of 6-mer widely spatially. Each class of such a matrix can be obtained by rotating each mask 90 degrees, after depositing one of four nucleotides. According to the conventional method, the following steps are needed for preparing each nucleotide. (i) The nucleotide (amino acid) solution to which (ii) conversion of the specific location of a base activated optically (expressed with the white part of drawing 10 A-10F) was carried out, and the excessive (iii) reactant made to react are washed through the hole of a mask. The complete cycle of such a wet chemistry method is repeated every, whenever it prepares a new nucleotide respectively.
In contrast with this, by the approach of this invention, all four nucleotides (or 20 amino acid) are spatially distributed on a front face widely, and all the nucleotides in a layer (amino acid) are only combined by the wet chemistry method after that by it. For example, the mask shown in drawing 10 A has one square big hole (part with which it is expressed white), in the 1st cycle which deposits the first nucleotide in the pair NETO real library of a 6-mer nucleotide, an adenosine nucleotide passes this one square big hole, and electrostatic atomization is carried out on a base. Then, whenever it deposits the nucleotide of other three cytosines, a guanosine, and thymidine, a mask is rotated 90 degrees, and the layer of the first nucleotide is generated every four quadrants of the base equivalent to the deposit of various nucleotides. After the chemical bond of the deposited nucleotide, the next layer of a nucleotide is deposited using other masks, rotates a mask by a unit of 90 degrees like the case where the first mask is used, and carries out electrostatic

atomization of each nucleotide. a series of masks of drawing 10 A to 10F -- respectively -- being continuous (sequence not being asked) -- by using it, all possible things are generable in the combination of a nucleotide. It can be used for deposition of a up to [the dielectric base of the photoconductivity of a nucleotide with which what was shown in drawing 10 A-10F, and a similar optical mask were also charged].
Although chemical association of the nucleotide to an oligonucleotide end group is performed after depositing all four nucleotides and considering as a layer, it is carried out by raising temperature using the conventional method of the solid state chemistry which combines a nucleotide with the reactant activated by using the approach of placing a deposit into the ambient atmosphere of the solution steam made into the saturation state, or activating other known chemical reactions. Thus, deposition of electrostatic atomization promotes composition of the matrix of an oligonucleotide at least 4 times, and it also promotes composition of the library of a peptide so that extent may become large a little (to about 20 times). Extensive manufacture of such a library is needed for investigation of gene analysis and a new drug etc. Especially DNA sequencing by compound-izing of the matrix of such a combination of the overlapping DNA fragments is one of the most interesting application of the matrix which combined the oligonucleotide. Furthermore, this invention means the equipment with which the spraying object of the charged particle by which electrostatic atomization was carried out is led to the part which should be deposited by the electric-field place.
Drawing 24 shows the equipment which has the electrostatic atomization chamber 100 which contains the base holder 69 which supports the base (reference is impossible in drawing 24) with which the capillary tube 52 with which the spraying object of a particle charged electrically is discharged, a protect ring 20, the grid-like electric shielding plate 70 which is helpful for enclosing and leading the spraying object of a charged particle, and a deposit are made inside. It is suitable for this holder 69 to have the bearing and another magnet (for it not to be visible in drawing 24) which rotate with the magnets 201 and 202 which rotate with the step motor 200 driven by the driver 205, and it is suitable for it to rotate these magnets 201 and 202 further with the step motor 200 driven by the driver 205. It is isolated electrically [a chamber 100] and the driving gear of this magnet attenuates vibration.
In order that laser 300 may make a laser beam 301 irradiate beside an electrostatic atomization chamber so that the electrostatic atomization chamber 100 may be passed and it may result in a microscope 302, it is suitable for it to have a transparent aperture 101 and a transparent hole (for it not to be visible in drawing 27), or the grid-like electric shielding plate 70 to which the plastics aperture was attached. Thereby, the "torch-like thing" of the charged particle emitted from the capillary tube 52 can be observed now. This laser 300 is Ne-Ar laser, and it is suitable for a microscope that there is one 10 times [5 to] the scale factor of this.
Transfer pipet 400 is connected with the chamber 100 with the tube 402.
This is used for a solution, pouring in so that the spraying object of a charged particle may be generated. supply of the dry air (other gas again) from a tank 500 -- a tube 502 and a flow meter 503 -- a passage -- a chamber 100 -- flowing . It is suitable for a hygrometer 505 to have the sensor 506 arranged in the chamber. The particle of a spraying object, and since typically adjusts the boil off rate of the drop of a water solution, it should be controlled by this humidity.
Humidity should be kept typical to about ten to 30%. Furthermore, by this illustrated tank 500, dry air can be obtained with silica gel. A flow rate is a part for 200-500mL/standardly.
The dual power source 700 impresses the electrical potential differences Ug and Uc of the range of a kilovolt to the components inside a chamber as follows. It is suitable for a current to measure with the nano ammeters 702 and 705, respectively. An electrical potential difference Ug is given to a protect ring 20, and an electrical potential difference Uc is impressed to a capillary tube 52. Or it is also possible to use the single power source connected to the protect ring 20 and the capillary tube 52 again. It is set as potential both repel [potential] the spraying object of the charged particle emitted from the capillary tube 52.
Drawing 25 illustrates a detail from that of the electrostatic atomization chamber 100. This chamber 100 is set on the base 110 in which a step motor 200 and magnets 201 and 202 were formed and where the bottom was opened wide. The magnets 111 and 112 which correspond by these are driven, and the surroundings of the bearing 113 equipped with the sample holder 69 are rotated.
The guard shield plate 30 (illustrated by drawing 29 A and 29B) is stood on the sample holder 69, and supports the grid-like electric shielding plate 70 (illustrated by drawing 27). The thing containing the foot of four tubes made from an acrylic, the ring 32 made from polystyrene, and the top plate 31 made from Teflon that the hole 35 is opening in the center is suitable for this.

The top plate 31 is deforming a little so that it may illustrate, and what has a crater caudad is suitable.
Right above the guard shield plate 30, there is a convergence ring 40 arranged inside the grid-like electric shielding plate 70. This convergence ring 40 is hollow, and as shown in drawing 24 , that upper limit section is connected with the dry air tube 502. It is suitable for this air to pass along the tube 42 made from stainless steel partially covered with the tube 43 made from silicon exactly, to pass along the splice 44 made from polyethylene, and to be connected with the tube ring 45 made from silicon in the air. The smaller tubes 46 made from Teflon (trademark) have gathered towards the central open section from this ring 45.
It is suitable that the copper ring 47 is arranged at the central open section, and is arranged on the hole 35 of the guard shield plate 30. Although this tube 42 made from stainless steel is electrified with the electrical potential difference Ur from a power source (not shown in drawing 25 and 28), this electrical potential difference can be impressed through the lead wire which passes along one of the tubes 46 made from Teflon. This electrical potential difference Ur may be used as an auxiliary means for turning a charged particle in the predetermined direction. Instantiation-like [this] only although this electrical potential difference is shown as what is impressed through one alligator clip.
It is suitable for the electrical potential difference Ur on the copper ring 47 to consider as a middle value with the electrical potential difference of the capillary tube 52 with which the electrical potential difference of the sample holder 69 (and the base supported by this, drawing 3 , and 4 reference) and the electrical potential difference Uc are impressed so that it may mention later.
It is suitable for this grid-like electric shielding plate 70 to have been knit with the cloth for the electric shielding made from a polo propylene of a 1000-micron hole, and this [its] is available as trade name CMP-1000-A of Florida, the Miami rake, and a small parts company. This hole should be made about 1.0 to 1.5 mm, and this matter should be a good dielectric. It is suitable for an aperture 71 that it is a product made from an acrylic plastic because of the optical property which lets light pass. Although the grid-like electric shielding plate of another funnel mold is shown in drawing 16 A, about this, it mentions later.
In addition, it is suitable for the grid-like electric shielding plate 70 interior that it is the glass capillary tube 52, and the capillary tube holder components 50 are shown best at drawing 26 . The liquid sprayed reaches from a tube 402 (shown by drawing 24), and reaches a capillary tube 52 through the tube 53 made from the brass of nickel plating, and is breathed out from the orifice of the glass tube 52 extended and formed. The outer diameter of the hole of a capillary tube 52 should not exceed 30 - 40 microns, but surface treatment of the outside front face should be carried out to the hydrophilic property. The solution discharged is charged with the lead wire made from high grade platinum inserted through the hole of a capillary tube 52, and an electrical potential difference Uc is electrically impressed to this lead wire through brass, an iron tube, and a typical alligator clip from a power source 700 (drawing 24). this protect ring 20 is arranged near the upper limit section of the grid-like electric shielding plate 70 -- it is only the thing of the shape of annular or a doughnut.
Drawing 30 shows the components of the sample holder base 69. Upper components rotate on the bearing made from brass welded to the brass plate 698, and fix the acrylic plate 693 through a spacer 695 on a brass plate. Driving magnets 111 and 112 are set on the acrylic plate 693. The assembly components 691 of a mask are supported by the auxiliary holder 692 made from an acrylic exactly joined to the plate 693. A bearing 697 and a spring 699 serve as assistance of exact positioning.
The sample holder 69 at the time of deposition needs to be rotated in order to obtain a uniform deposition film, when the flow rate of air is low.
Drawing 31 shows the sample holder which suits the sample holder base 69 shown in drawing 30 .
This auxiliary holder 692 is set on the plastics plate 6922, and it is equipped with this plastics plate on the base 6923 which has a handle 6924, and it arranges a sample holder in the area divided with the brass plate 698, the spacer 695, and the acrylic plate 693. For example, in order to perform electric contact to the electrostatic equipments 581 or 621 of drawing 4 A, or electrostatic equipment like 95 of drawing 4 B, it is suitable to use a carbon paste.
Drawing 32 A shows one suitable example of this invention, and it is used in order for rocking equipment to make the capillary tube 52 of electrostatic atomization vibrate or rock. It is suitable for this electrostatic atomization holder 50 to make it rock according to the device 252 connected with the motor 250 and the brass tube 53 (or the components besides something of the capillary tube holder assembly 50) which are made to rock for a reciprocating motion or rotation. This device 252 is arranged to the tube at the right angle. It is suitable to design this device suitably and to make it only the time amount same above each area of a base 58 make the tip of a capillary tube 52 stay.
A certain approach of others which vibrate a capillary tube also enters within the limits of this invention.

Moreover, the example of drawing 32 A also shows the typical structure for manufacturing the matrix containing two or more spots. In this example, after depositing each compound, the sample holder 69 and a base 58 move to Y as horizontal X. Generally these are perpendicular to a motion of a charged particle 56. In the example of drawing 32 A, a bearing 113, magnets 201, 202, 110, and 112, a step motor 200, and the driver 205 of drawing 25 are not used.
This migration is made by the X-Y flat-surface migration stage which can also be made what kind of type. Although, as for drawing 32 A, the flat-surface migration stage which has the micrometer heads 121 and 122 of X-actuation with a vernier and Y-actuation shows the thing of the type operated manually, this flat-surface migration stage may be an automatic thing which can also make what manual type of thing, and is driven by a step motor or what is equivalent to it, the contact switch, the circuit, or the computer program.
** fixes the sample holder 69 using a magnet 115 on a flat-surface migration stage with electrode 102 arranged between a magnet 115 and a base 58.
Moreover, this invention also generates a deposit in a different geometric array from the place mentioned above. For example, it can also arrange along with the circle of a different radius using theta and r flat-surface migration stage, i.e., the rotator, instead of X and Y flat-surface migration stage.
This flat-surface migration stage moves a base so that the hole of a mask may move to a new location [above a base]. The new matter can be made to deposit on new deposition area. Thus, the deposit of the shape of a matrix of various matter can be arranged in accordance with a line and a train.
Drawing 32 B expands the circular part of drawing 32 A, and shows the hole 60 of a mask 62 and a mask, a base 58, and a deposit 64. Although it is suitable for the mask reinforcement beam 61 shown in a sectional view to consider as thin ** which fixed on the top face of a mask 62, the thing of the shape of a grid like a honeycomb etc. is sufficient as it. A spacer 6258 is installed between a mask 62 and a base 58. It is suitable for this spacer 6258 that it is a small solid sphere so that a mask 62 can rotate in every direction on the front face of a base 28.
Drawing 33 shows other examples of mask migration equipment, and is equipped with the 1st plate arranged movable in the direction of X on the 2nd plate 126, and this 2nd plate 126 is movable in the direction of Y on a base plate 127. The bearing of X of the gestalt of cams 123 and 124 and the rocking equipment to the direction of Y is carried out to plates 125 and 126, respectively. If these cams rotate, these plates will move. This mask migration equipment can also be installed on the rotation base of the sample holder 69 of drawing 25 .
Every time drawing 34 removes the point that the diameter of the rotation sample holder base 69 being large and deposition are performed at one side (right-hand side of drawing 34) of a chamber 100, it shows the chamber 100 similar to drawing 25 . On the other hand, this mask 62 is electrostatic equipment (drawing 34 does not show).
He is trying to pour in an electric charge by the discharge style of the reversed-polarity ion 856 from the corona electrode boiled and connected. Since it has a polarity opposite to a charged particle, this reversed-polarity ion is called in this way. For example, since drawing 34 is a polarity negative in reversed-polarity ion, it is shown that the charged particle deposited on the base 58 of a dielectric is a forward polarity. It is suitable for this corona electrode that it is a thing including the array of microelectrode.
In order to prevent the electric field from the corona electrode 850 which blocks the flow of the charged particle 56 from a capillary tube 52 to a mask 62, it is suitable for this corona electrode 850 to surround with protection shielding like ground Faraday shield 840, and it can ground this shielding. The bottom of this shielding 840 is opened wide and arranged near the mask 62. Arranging directly under a table 69 is suitable for the counter electrode 842, and this is easy to complete the Faraday cylinder and surrounds some bases with a metal. However, it is suitable for this counter electrode 842 to connect the electrical potential difference which draws the reversed-polarity ion 856 and is moved to the downward mask 62 to the electrostatic equipment (not shown in drawing) which carries out a seal of approval, without [instead] being grounded.
Although it is suitable for the 2nd counter electrode 844 to arrange to the table 69 down side of the lower part of a capillary tube 52, it is prepared in the opposite side in the 1st counter electrode 842 to the axis of a table 69. It is suitable for the 2nd counter electrode 844 to consider as a polarity with the opposite 1st counter electrode 842 like the capillary tube 52 of electrostatic atomization.
With the equipment of drawing 34 , in order to prevent the electric-field place from the counter electrode which reaches a mask 62, a rotary table 69 should not be made metal. It is suitable for this rotary table 69 that it is made of plastics or a dielectric like a mica.
Although this invention has generally been explained, with reference to the following examples shown in

drawing, he could understand this invention more easily. However, these do not limit this invention.
Example 1 The ground of the single fiber which has many holes in the water solution of 0.01% of horse myoglobin (a sigma company, St. Louis) was passed, and electrostatic atomization was carried out on the front face of the conductivity of glass.
This electrically-conductive-glass front face was prepared by processing microscope slide glass with SnCl4 steam in a furnace. + The seal of approval of the 5kV is carried out to the capillary tube of electrostatic atomization, and in order to use a polypropylene fiber as a mask and to make it deposit on an electrically-conductive-glass front face, electrostatic concentration of the electrostatic atomization was carried out.
When drawing 5 A is compared with 5B, it turns out to the magnitude of the hole of fiber being 22 - 23 microns that myoglobin protein is deposited as a spot with a magnitude of 5 - 7 microns, and there is the electrostatic-lens effectiveness so that clearly. It is observed that the particle of the dust which the spot in which some in a pattern failed has in some places is the cause, and, as for this, exists on an electric shielding plate. In this example, it became clear that protein can be deposited on coincidence as many spots. Thus, the thing with which it was covered at the spot of a large number estranged at intervals of about 47 microns and which is included for the spot of 1.8x105 protein in the location of the glass base of 2 became clear 20x20mm.
Example 2 It let the hole of a Teflon electric shielding plate (mask) pass, and electrostatic atomization of the methanol solution of nine kinds of different coloring matter (0.01%) was carried out on the front face of a porous IMMOBILON-P filter (Millipore Corp.). The front face of this filter gave conductivity slightly by dipping a polyethylene glycol -8000 in a solution (MgCl2 of 10mM, and glycerol 15%) 15%. At intervals of 4mm, through the Teflon mask with a hole of 100 individuals with a diameter of 0.5mm, the seal of approval of the +7kV was carried out, and deposition of electrostatic atomization performed it to the capillary tube. After depositing 0.5 microliter of each solution at a time, the mask was moved only about 0.6mm and other coloring matter was deposited. The wafer of the IMMOBIRON-P filter of porosity including the matrix of the spot of deposited coloring matter is shown in drawing 11 . According to the approach of this invention, this example deposits two or more matter on a base according to a predetermined pattern, and can manufacture many the samples for multi-analysis and libraries to coincidence.
Example 3 The conditions of the electrostatic atomization used in this example resemble what is used in the example 1. Electrostatic atomization was carried out on the front face of a ** of the two-kind the nitrocellulose filter which let the hole of a polypropylene mask pass and became wet for a while in it about protein, a commercial peroxidase, and commercial alkaline phosphatase (a sigma chemical company company, cent Lewis, Montana) dialyzed with distilled water. It deposited on the predetermined pattern by electrostatic atomization, and although protein held the combining ability and the enzyme reaction of the functional property, i.e., a proper with natural ligand, it became clear.
The pattern of the deposited enzyme is not visible on the front face of a membrane filter after electrostatic atomization. However, by dipping the membrane filter on which the peroxidase was made to deposit in the base (available from the sigma company of 3 and 3'-diaminobenzidine, an abbreviated name DAB, and Montana cent Lewis) of a standard peroxidase, the pattern of this enzyme can be seen now by the eye, and serves as a gestalt of the insoluble product of the brown in a peroxidase reaction as a result. The array of the spot which shows existence of an insoluble product is shown by drawing 12 A.
It was visualized, as similarly the membrane filter which deposited alkaline phosphatase on it was dipped in a standard alkaline phosphatase base (the system kit of a 5 BUROMO-4 chloro-3 Inn Dolly phosphoric acid / nitroblue tetrazolium base, a sigma company, cent Lewis, Montana), and the insoluble blue product by the alkaline phosphatase reaction was generated as a result and this pattern was shown in drawing 12 B. This result shows that the enzyme activity of alkaline phosphatase and a peroxidase is maintained also after electrostatic atomization deposition.
Example 4 It deposited in electrostatic atomization on the IMMOBILON-P membrane filter which passed the mask which has two or more holes for various antigens (Homo sapiens and bovine serum albumin, an ovalbumin, Homo sapiens hemoglobin), and became wet. After depositing each of these protein antigens, this mask was moved every 1.1mm. After all four deposition of a protein antigen, this membrane filter was dried for 15 minutes at 37 degrees C, and it blocked by dipping in 0.05% of Tween-20 and the albumin (ovalbumin) PBS solution (the sodium phosphate buffer of 10mM, pH7.2, 0.9% of NaCl) of 1% of hen. After blocking, this membrane filter was dipped in the goat antibody solution (it dilutes with a sigma company and 1:1000) to a human serum albumin for 1 hour. then, it dipped in the solution of the IgG antibody to the goat by which washed this filter twice [every / during 10 seconds] with PBS buffer solution, and the indicator was carried out with alkaline phosphatase (it dilutes with a sigma company and

1:3000). After washing the antibody to the excessive goat in PBS, this filter is recognized by producing an insoluble product, as the example 3 explained by dipping the deposition of a spot by which the indicator was carried out with the enzyme in the solution of an alkaline phosphatase base. Drawing 13 shows the pattern obtained by using this micro ELISA analysis method. The spot equivalent to deposition of a human serum albumin is the most intense color so that it may be expected. what does not have an intense color like bovine albumin or Homo sapiens hemoglobin because of [for an ovalbumin or the cross-reactivity of some Homo sapiens albumin antibodies / as opposed to bovine albumin probably] contamination by the Homo sapiens albumin in a Homo sapiens hemoglobin sample, and ** -- the spot of other protein [like] cannot be seen at all. this example shows that the procedure of electrostatic atomization does not change the property as a proteinic antigen notably, and is ****** about application of an electrostatic atomizing process about extensive manufacture of the immunity enzyme probe of two or more components.
 example 5 The protein film for mechanization study-analysis was manufactured by the electrostatic atomizing process. One rectangular hole was passed and electrostatic atomization of the 2mg [/ml] concanavalin A (sigma company, cent Lewis, Montana) solution containing a 0.5mg [/ml] glycerol was carried out on the aluminum electrode covered in the macromolecule conductivity auxiliary layer with a thickness of 2 - 5 microns.

This auxiliary layer was created by drying the film of the mixed water solution of every 3% of three compounds (a polyethylene glycol -8000, Pori (anethole sulfonic acid) sodium salt, and Triton X-100), respectively. The seal of approval of the electrical potential difference of 4.0kV was carried out for this protein solution to the capillary tube, and electrostatic atomization of the current of 33nA was carried out from the capillary tube tip installed in 20mm of upper parts of a sink and a base. Deposition was performed for 10 minutes among dry air. After electrostatic atomization deposition was carried out, the crosslinking bond of this sample was carried out for 15 minutes in 25 degrees C and 25% of glutaraldehyde (Aldrich, Milwaukee, Wisconsin) steam. When waterdrop was poured on the base front face, this sample separated and lost touch with a base in 5 seconds. In order to create the microphotograph of this sample as shown in drawing 14 A, this sample was paid by waterdrop and the processing using the Qu Massey brilliant blue R (sigma company, cent Lewis, Montana) solution covered with the cover slip colored it.

The film of alcoholic dihydroGENAZE (LADH, a sigma company, cent Lewis, Montana) of the horse liver shown in drawing 14 B was manufactured on the aluminum electrode covered in the auxiliary layer which consists of 95% of sodium alginate salt (a sigma company, cent Lewis, Montana), and 5% of surfactant Triton X-100. From the capillary tube installed in 15mm of upper parts of a base, this LADH solution containing 5mg [/ml] protein and 1.5mg [/ml] cane sugar is +4.3kV and current 30-40nA, and carried out electrostatic atomization in dry air. Thus, the crosslinking bond of the deposited film was carried out in 8 minutes with 28 degrees C and 25% of glutaraldehyde steam. Then, it is this sample 0

Each capacity about change of the isometric tension to the NADH solution of 4mM(s) was inspected. It is shown that the protein according [the increment in the isometric tension of the film by the deposition of electrostatic atomization in which induction was carried out by 6 - 8% of same ligand, and the film prepared by the conventional approach] to an electrostatic atomizing process holds change of that structure as a result of the function in which ligand and a proper join together, and this association.

These examples show that it can manufacture by deposition of electrostatic atomization, without losing the functional activity for a protein sample with important uniform small thickness, in order to inspect protein by the mechanization study-approach.

Example 6 Deposition of the protein from the protein solution condensed in the desiccation ambient atmosphere becomes the gestalt of a vesicular structure as a result. Drawing 15 A expresses the image by the atomic force microscope (AFM) of the Homo sapiens hemoglobin film deposited on the electrode of the ground gold. Electrostatic atomization of this protein was carried out from the water solution containing Homo sapiens hemoglobin 0.6mg/ml which is not adding other additives. Deposition impressed the electrical potential difference of +5.3kV to the capillary tube installed in the distance of 20mm of upper parts of a base, and performed the current of 12nA in dry air as a part for flow rate 100nl/of a sink and a solution. This image expressed to drawing 15 A shows existence of the protein cluster to the magnitude of about 300nm. If it puts to the damp air (they are for 20 minutes and 100% of relative humidity at a room temperature), a big cluster will disappear as a result and it will become the gestalt of a flat front face with thin "channel" observed as the black structure of the image shown by drawing 15 B. It explains that drawing 15 C has the high permeability of the protein film deposited in electrostatic atomization. In this example, the small wafer of solid coloring matter was put on the front face of both the film deposited in electrostatic atomization, and the dried film, and these films were put into the chamber of 100% of humidity in it. Under

existence of water, a coloring matter molecule permeates this protein film, and forms the location of the concentric circular color diffused around each wafer of coloring matter. As shown in drawing 15 C, diffusion of this coloring matter advances quickly numbers of times with the film made to deposit in electrostatic atomization compared with the film created by drying the protein solution which is a conventional method. When manufacture by deposition of electrostatic atomization dries this example from a solution, it explains creating the matter of new porosity from the matter which forms a film ****** to homogeneity. Moreover, how to adjust the permeability over the specific ligand of the film deposited in the electrostatic atomization after the deposition by "baking (baking)" in porosity, i.e., the ambient atmosphere containing a solvent steam, is explained. By this, ****** which extends relative spacing of the protein molecule within a cluster comes be made.

Example 7 The lambda-DNA stock solution (product of a new British biotechnology lab) containing DNA0.5micro g/mu l was diluted twice with water, and after denaturalizing by boiling for 5 minutes, it quenched on ice. 10micro of this solution l was put into the capillary tube, and electrostatic atomization of the 1microl of them was carried out by the electrical potential difference of +4.9kV, and current 40nA using the lead wire of platinum into which it was put by the capillary tube as an electrode. Deposition let the electric shielding plate (mask) knit with the polo propylene which has a rectangular hole (type E-CMP -250, a small parts company, Florida) pass, and in order to make a glass front face into a hydrophilic property, it was carried out on the front face of covering processed by plasma discharge. The wet O-ring which cut off Whatman, 3M, and a paper performed electric contact on a glass front face. The crosslinking bond was carried out by the UV irradiation for 15 minutes, it is 0.1% of SDS, and deposition of this DNA was rinsed, and was washed twice with water. Then, it is the boric-acid buffer solution of 0.1M and pH7.0, this slide was rinsed, and it put in into the succinyl oxide of 70mM, and processed for 10 minutes in the same buffer solution containing 35% of 1-methyl-2-pyrrolidinone (Aldrich make). then, boric-acid buffer solution washed this slide for 2 minutes, and the every water during 2 minutes washed it 4 times. The BIOCHINIREITIDO EcoRI digest of lambda-DNA which can come to hand from a sigma company was boiled, and it quenched on ice, and added to the compound-ized solution by the 100 ng/ml last concentration. The 4 time dilution SSC solution which contains a dextran sulfate salt 100microg [which carried out digestion from SDS and DNA of the testis of a salmon 1% //ml] 10% was used as (sigma company make) and a compound-ized solution. Compound-ization was performed by the homemade micro chamber for 62 degrees C and 14 hours. The two-fold-serial-dilution SSC solution washed this slide twice after compound-izing, and the dilution SSC solution washed for 5 minutes once 0.2 times, and it blocked with 2%BSA and AP buffer solution which contains casein 1% for 30 minutes after that. AP buffer solution is 0.

MgCl2 of NaCl of the TRIS-hydrochloric-acid buffer solution of 1M and pH 7.5 and 0.1M and 2mM and 0.5% of Tween-20 are included. AP buffer solution washed this slide for 5 minutes after blocking, and it was made to ripe in 25 minutes and in a 1microg [/ml] streptoavidin alkaline phosphatase joint (sigma company make) solution. Then, AP buffer solution washed the slide 4 times, AP buffer solution which adjusted pH to 9.5 washed, and it put into the standard substrate solution of alkaline phosphatase like an example 3. The array of the same spot as what was expressed with these drawing 12 A and 12B appears on glass as what directs concentration of the alkaline phosphatase in the spot of DNA for association of a BIOCHINIREITIDO DNA hybrid.

example 8 others -- in the experiment, electrostatic atomization of the lambda-DNA strange nature child manufactured as the example 7 explained was carried out on the nylon filter (gene screen hybridization filter of Du Pont) from the solution containing 20% of glycerol, and 0.01% of bromophenol blue coloring matter. In order that the bromophenol blue coloring matter of this latter may visualize the sprayed pattern, it is added before compound-izing and all coloring matter is extracted from a filter during pretreatment of compound-izing after that. Deposition was carried out in the damp glove compartment of 60% of relative humidity. This filter was installed on Whatman 3M damp paper which covers a carbon electrode, and covered this filter after that with the shelter knit with the same propylene as what is used by deposition of DNA on glass. Electrostatic atomization of the DNA solution of 2microl made into the purpose was carried out with the electrical potential difference of +(4.2-4.5) kV, and the current of 20-30nA. This DNA was calcinated for 20 minutes at 75 degrees C after deposition, and it denaturalized with the NaOH solution of 0.5M, and washed by the TRIS-HCL buffer solution of 0.5M, and pH=7.4, and the crosslinking bond was carried out for 15 minutes by ultraviolet rays. Then, compound-ized prior processing was carried out at 42 degrees C to the filter for 1 hour into the Denhardt solution of the SSC buffer solution of 6 time dilution, 45% of formamide, 1%SDS, 10% of dextran sulfate salt, and 5 time dilution, and the buffer solution

containing DNA of the testis of the salmon which denaturalized by 100microg [/ml] supersonic vibration. 42degrees C of compound-ization were carried out like the upper experiment for 14 hours within the solution which added the 200 ng/ml BIOCHINIREITIDO lambda-DNA probe. After compound-ized processing is the SSC buffer solution (5 minutes) of two fold serial dilution, and 0.
it washed twice at the SDS solution and the room temperature 2%, and riped every 15 twice at SSC of dilution, 0.2%SDS, and 62 degrees C 0.1 times after that. As AP buffer solution washes this filter after washing, and it blocks at a room temperature for 1 hour in AP buffer solution containing the mixture of 2% of bovine serum albumin, and 1% of casein, and is made to ripe with the solution of SUTOREPU avidin phosphatase association after that and the front example explained, it washed and riped within AP substrate. The array of the bluish spot similar to drawing 7 and the thing shown by 12A and 12B appeared, and the location deposited in the electrostatic atomization of lambda-DNA became clear.
Examples 7 and 8 maintain the function in which the DNA molecule by which electrostatic atomization was carried out does an interaction especially about a complementary DNA strand, and show that application of the electrostatic atomization technique over manufacture of the inspection based on DNA and a library is expanded.
Example 9 In this example, electrostatic atomization of the various coloring matter was carried out from the water solution using air. In order to carry out electrostatic atomization, the needle point of stainless steel was put in during jet of the compressed air breathed out from the nozzle of plastics. **(2-5) kV was impressed to the needle, and the high-voltage power source of antipole nature was connected to the metal plate. it covered with the 30x30cm Whatman 3M paper which became wet for a while on the metal plate, and covered with the plastics mask with a thickness of 1cm which has the array of a circular hole with a diameter of 13mm. The flow rate 0 of the solution sprayed the distance of 0.2-1m to a base in the electrostatic atomization which considers an air bleed as assistance
It carried out by part for 1-1ml/. Only slight distance moved this mask after one deposition of coloring matter, and the following coloring matter was deposited. The deposited pattern is shown in drawing 17 .
It is only different that a bigger sample (spot) deposits more quickly on a bigger area, and it is alike at other spots with a lot of [this and the thing received by use of only electrostatic atomization] matter. It explains that the fundamental phenomenon of the electrostatic concentration and the electrostatic concentration which pass a mask with two or more holes in addition to electrostatic atomization with this pure example, and patternizing can be used also with the means of others which generate a charged particle and a drop.
Example 10 The single fiber cloth with two or more of the same holes as what used 0.5% of pancreas RNAse (a sigma company, cent Lewis) containing 30% of cane sugar and 10% of glycerol (based on the dry protein weight) in the example 1 was passed, and electrostatic atomization was carried out to the conductive aluminum layer on a polymer base material. Within the closed chamber, electrostatic deposition impressed the electrical potential difference of +4.0kV to the relative humidity of 18%, the internal diameter of 10 microns, 10nA, and a capillary tube, and was performed for 10 minutes to them. Compared with the thing of an example 1, a lot of matter by which electrostatic deposition was carried out clarified capacity to manufacture the sample which has the three-dimensional structure. As shown in drawing 19 B, the array of 5 - 7 microns wide and the protein sample of magnitude with a height of 30 - 40 microns can be manufactured by the electrostatic atomizing process by this invention which uses the lens effectiveness in the hole formed by approaching a dielectric mask mutually so that it may illustrate to drawing 19 A.
Example 11 matter and approach Matter. The trehalose of alkaline phosphatase (AP) p-nitrophenyl phosphate (p-NPP base table setting, sigma first company) ** and cane sugar can come to hand from the sigma chemical company of Montana and cent Lewis. [of the intestinal mucosa of a cow] All other salts and additives for a buffer were the quality for analysis.
The design of the capillary tube for electrostatic atomization. The capillary tube for the electrostatic atomization of three different designs has been tried through this research. The 1st design shown in drawing 20 A resembles "the minute electrostatic atomization ion source (1994 besides WIRUMU, 1996)" plated with the silver larer instead of gold on the outer surface of a capillary tube. Surface treatment of the glass capillary tube which took up both ends was first carried out for 20 seconds and under reduced pressure by non-electrode plasma discharge (inside of the chamber of 0.01torr, the discharge power 10-20W, and the Pyrex class, 0.25L). After performing defecation by such plasma, it was activated in the hydrochloric acid (50 g/L) and the solution with which SnCl2 acidified, and this glass capillary tube was washed with water, and was covered in the silver "mirror plane" (1981 besides YAMPO risky). This design is called a capillary tube with an external electrode.
The 2nd design shown in drawing 20 B is deformation of the electrostatic atomization capillary tube

explained by this invention person's (1993 besides Morozoff) laboratory. Although the metal electrode (a tungsten or lead wire of stainless steel CHIRU) of this capillary tube is not put to a gas phase, it decreases the risk of the corona discharge under the high voltage. This 2nd design is called a capillary tube with an internal electrode.
By the 3rd design of a capillary tube (called a bridge capillary tube), contact to a protein solution and a metal electrode is completely avoided by introducing a liquid bridge between them. As shown in drawing 20 C, the front face of the outside of the stainless steel tube 4 is used as an electrode put to the interior of the far edge of a big external capillary tube. Although the conductivity of this external capillary tube will exceed 100 conductive times of an internal capillary tube and most currents will flow the big external capillary tube 5 since the cross section of the external capillary tube 5 is larger than that of the internal capillary tube 7 10 or more times, on the other hand, it is used for the internal plastics capillary tube 7 supplying a protein solution.
The transfer pipet pump (KOREPAMA, NAIRUZU, Illinois) which combined the Hamilton micro transfer pipet of 10microL controlled by the microprocessor was used in order to supply a solution to the capillary tube of electrostatic atomization. The flow rate was made into 6-9microL/h, and the external diameter at the tip of a capillary tube was changed in 50-100 micrometers in various experiments.
A chamber with a humidity control function. In order to protect a protein sample from contamination of the dust particle which exists in surrounding air in order to adjust humidity during the experiment of the electrostatic atomization of an enzyme, electrostatic atomization deposition was carried out with the box with the almost small (0.5L) product made from an acrylic of a rectangular parallelepiped shown in drawing 21 in diagram. The glass window is attached beside [one] this box so that the thing of the shape of a torch of electrostatic atomization and the base under a stereoscopic microscope can observe vividly. Measuring at humidity, the humidity and temperature in a chamber measured them by the digital sensor (the Fischer company make) with a precision of 0.2 degrees C at temperature 2 to 4% in the steady state. In order to improve responsibility of a sensor and to make humidity of all parts the same within this chamber, inner air was stirred by the small fan. The dry air from a tank or the air which bubbled water and the shelf was made to ****** was introduced in the chamber until it reached required humidity. Then, this fan was stopped and electrostatic atomization was started. During the spraying experiment, when it deviated from the level which needs humidity 3 to 5%, the gas which dried or became wet was added.
Mass measurement of the protein deposited in electrostatic atomization. The homemade Xtal crystal minute balance (QCM;)
SOL BUREI and 1959 were used and the mass of the protein by which electrostatic atomization was carried out was measured. This minute balance is made of the Xtal crystal (12 to 17 MHz, with [of silver with a diameter of 5mm] an electrode) of an AT cut with which it is marketed after removing a protective plate. 0.1% of sugar water solution performed the calibration of QCM. The minute drop of this solution from which capacity changes between 0.25 - -1.0microL was dropped in the middle of the Xtal electrode using the transfer pipet pump with the micro transfer pipet of Hamilton 10microL, and it dried as a spot of an one to 1.5 mm diameter. It was made to dry further by the flow of desiccation nitrogen or dry air until it would introduce in the chamber which closed this Xtal and the resonance frequency observed would not change, after a solvent evaporated under the flow of surrounding air. The difference between the resonance frequency in a beautiful crystal and the resonance frequency in the crystal of the spot of dry sugar was calculated for every mass of sugar. Although the calibration curve was linearity in the range of 0-2microg, there was 2 - 3% of deviation of an experimental value from linear regression. Since sensitivity is more small, in order for an electrode periphery to decrease the variation in an experimental value about mass deposition, it should be made to deposit on the core of the Xtal electrode (SOL BUREI, 1959).
Electrostatic atomization deposition of the protein to the Xtal electrode top was carried out so that it might illustrate to drawing 21 .
この電極はアースされ、電極の中心部の上に位置する孔が付いた、テフロン®また

はパラフィルム®からできているプラスチック遮蔽プレートを、結晶上に乗せた。

It dried until it put in this Xtal crystal in the desiccation chamber of QCM after proteinic deposition, and it connected with the oscillator circuit and vibration frequency became fixed. Then, bias of the resonance frequency of Xtal determined the dry weight of this protein deposit using the calibration curve. Therefore, it was determined that the solution of 1microL is dried on the Xtal electrode, and that concentration of the protein in dialyzed AP solution will measure the mass of the residue dried as explained in the top.

Measurement of the specific activity of AP deposit. The desiccation powder (sigma chemical company) of AP marketed is dissolved in water by the concentration of about 1 mg/mL, and it is a night and 10-5M. It dialyzed to the solution of MgCl2 and pH 7-8, and at-long-intervals alignment separation was carried out by 3000xg for 1 to 2 minutes, and it held at -20 degrees C. This stock solution was thawed before the experiment, and it diluted 5 times with water, and centrifugal separation was carried out again. The capillary tube of electrostatic atomization, a tube, and micro transfer pipet were filled with the protein solution. By this approach, it is strict prohibition to put a bubble into a solution.
Typically, in each deposition, electrostatic atomization of the protein solution of 1microL was carried out. As mentioned above, the proteinic spot was extracted 3 to 4 times after measuring the dry mass of this deposit by the drop of 1-2microL of buffer solution (0.2 M TRIS/HCL buffer solution, pH9.5, 1mM MgCl2, 0.1%Tween20). Then, these extracts were mixed, and it diluted so that it might become the volume of 40microL with the same buffer solution. In the electrostatic atomization of a protein solution, when a hydrocarbon existed, the protein weight in a solution calculated, having assumed that the ratio of a protein-hydrocarbon did not change depending on electrostatic atomization.
The activity of AP was measured immediately after adding the extract solution of 5-20microL to p-NPP solution 1.0mL of the TRIS/HCL buffer solution created with the tablet of a sigma first company. Activity is a room with a thermostat and was measured at the temperature of 25**1 degree C.
It turned out that it depends on enzyme concentration for the activity which measures record by 410nm, measures absorbance in 2 - 5 minutes with the spectrophotometer (AVIV, form 118DS) by which computer control was carried out, and is determined by linear regression analysis linearly. This specific activity was calculated using the protein concentration measured by gravimetric analysis as the upper mass test section explained.
In a series of the deposition experiment of each, the specific activity of AP in the solution prepared for electrostatic atomization deposition and the dry sample was measured. AP solution of 1microL was directly put on the Xtal electrode, and, in the case of the latter, it dried by the flow of air. Although it dried, this deposit was extracted after measuring mass, and that activity was measured like the place explaining the sample which is this and which was deposited in electrostatic atomization.
Effectiveness of a hydrocarbon. After desiccation, in order to investigate the effectiveness of recovery of the AP activity of cane sugar and trehalose, the minute drop (5microL) of diluted AP solution was dropped on the glass front face, and the water solution containing the water of tales doses or a different hydrocarbon of an amount was added to each drop. The fully mixed drop was dried within the oven under the reduced pressure made by the water pump. Then, it was made to dissolve, as the spot of electrostatic atomization deposition explained the dry spot, and those activity was measured.
A result and examination Measurement of the mass of the sample made to deposit in electrostatic atomization. The shift of the resonance frequency of the Xtal vibration determined the deposited mass. However, the visco-elastic property of the element of not only the mass of a deposit but others, especially a deposit affects change of vibration frequency. The protein sample of the electrostatic atomization deposition obtained under various humidity conditions has a notably different internal structure and pack density. If humidity A is created at 50% or less, these will serve as opacity or opalescence, and if the electrostatic atomization deposition of the humidity A is carried out at 70% or more, it will be in transparence or the condition of not being completely visible (what is obtained by desiccation is resembled). Possibility that such a structural change would do to QCM measurement of the mass of a deposit was inspected in the special experiment. After measurement of the resonance frequency of Xtal of the dry electrostatic atomization deposit obtained with low humidity, A put Xtal of this deposit into the Petri dish for 30 to 60 seconds at 100%, and it was dried again, and resonance frequency was measured again after that. Although, as for the deposit of opalescence, the condition changed to the transparent film as a result of this processing, the number of resonance shocks did not change depending on this change. With the electrostatic atomization deposit under the condition of different humidity, it is thought that change of the structure which can be observed does not influence mass measurement.
Effectiveness of electrostatic atomization deposition. The effectiveness of this electrostatic atomization is defined by the ratio of the dry mass of the sample deposited in electrostatic atomization, and the dry mass of the sample of the protein which dried the volume of the tales doses of the same protein solution. This value shows a remarkable dependency to the design of the capillary tube of the electrical-potential-difference:V (4) electrostatic atomization used by the distance:h(3) electrostatic-atomization deposition from the diameter:d(2) capillary-tube tip of the hole passed when (1) sample deposits to the Xtal electrode. In a typical geometric parameter, h= 10-15mm, d= 2mm, and low-battery V=+(3-4) kV, the effectiveness of this

electrostatic atomization deposition changed from 60% among 80% depending on the design of a capillary tube, as shown in the result of Table 2. The leakage of the protein solution included in a liquid bridge can explain the thing with a little low effectiveness of the capillary tube of a bridge type because AP has pH=4.4 (INGUSUTOROMU, 1961). AP molecule will be charged in negative, if pH becomes larger than 4.4, and it should move toward the just charged electrode in these experiments.
Table When electrostatic atomization is carried out using a capillary tube which is different on the effectiveness of 2 electrostatic-atomization deposition, and the same conditions 1 Percentage of the thing recovery in the specific activity of AP

	内部電極	外部電極	ブリッジ型
活性[2] %	５５±１０	３２±９	３１±１２
効率[3] %	７９±７	７８±８	６２±９

1 Electrical-potential-difference V=+(3-4) kV of a capillary tube, current I=1-50nA A part for flow rate [of 0.1micro] L/, distance of 10mm from the tip to the Xtal front face A= 65**5% of humidity of an electrostatic atomization chamber.
2 A ratio with the specific activity of AP which carried out electrostatic atomization deposition with the specific activity of AP of an early solution.
3 The mass of the sample which carried out electrostatic atomization deposition, and protein in the solution by which electrostatic atomization is carried out Ratio with mass.
In deposition of the electrostatic atomization from a capillary tube with an internal electrode, effectiveness does not show a dependency at all with humidity. In the case of V= 3-4kV, in the situation of having changed humidity from 10% to 90%, the effectiveness of electrostatic atomization deposition of the average of 48 independent measurement or more was 74**6%. When the electrical potential difference was made to increase to 6-7kV, the effectiveness of electrostatic atomization deposition became 100% as a result.
Specific activity of AP deposited in electrostatic atomization. The ratio of the percent of the specific activity of AP after dissolving the deposit of electrostatic atomization, and the specific activity of AP in an early solution is used as a standard of maintenance of the original property of the protein in electrostatic atomization deposition. damage with AP big as shown by the data explained by drawing 18 A and 18B, when electrostatic atomization deposition is carried out under the high voltage (7-8kV or more) and the conditions of a high current (500-1500 or more nAs) -- wearing -- and the activity -- all are almost lost. The following factors are considered to bring about AP inactivation under these conditions.
(i) Inactivation by the result of the inactivation (iv) desiccation by the result of the collision with the electrode of the inactivation (iii) target by the result of the reaction of the corona-discharge product in the inactivation (ii) gas phase inside the electrostatic-atomization capillary tube by the electrochemical reaction which occurs on an electrode The last factor (iv) has the same effectiveness as the case where it is made to dry directly, and is expected that the design and the current of a capillary tube are unrelated. When it is made to dry directly on the glass under a vacuum and is made to dry by the flow of air on the electrode of the silver of QCM as shown in drawing 18 A, and 22 and 23, in the electrostatic atomization deposition from a capillary tube with an internal electrode, AP is inactivated with A= 65% of humidity, and 50 or less nA of currents (to about 45%). Under the same current and the situation of humidity, when electrostatic atomization deposition is carried out by the design of other two capillary tubes, AP is inactivated more notably (please refer to Table 2). (to 70%)
If an electrochemical reaction assumes the predominance of the capillary tube exceeding a capillary tube with a liquid bridge with an internal electrode to be the factor of the main damage in electrostatic atomization deposition, it will be being unable to expect and being unable to explain. As the curve of the lower part of drawing 18 A and 18B shows, a capillary tube with this internal electrode is difficult also for explaining that there is less damage notably than a capillary tube with an external electrode by the electrochemical reaction in a capillary tube to the bottom of all electrical potential differences and the situation of a current. The low current measured and compared the activity of AP deposited from the capillary tube the exterior and with an internal electrode before and after electrostatic atomization deposition of current 1500nA from the same capillary tube. The electrostatic chemical product which oxidized directly with the electrode or were collected in the capillary tube of AP damaged with low pH by oxidation of the

water in a capillary tube resulting in decreasing the activity of continuous electrostatic atomization deposition is expected. AP of the intestines of a cow is irreversibly inactivated by putting to 4.5 to 5.0 or less pH (1979 besides MAKUKOMU), and pH can be dropped to pH=3-4 at estimate besides Van BAKERU (1979) under the situation for current I=250nA and flow rate [of 1micro] L/. However, in both molds, a difference remarkable in the specific activity of AP of the deposit between the former and the latter is not looked at by the capillary tube of electrostatic atomization. Therefore, it is thought that inactivation of AP under the high voltage and a high current has broken out in the exterior of a capillary tube as the result of a reaction with the product of corona discharge or a result of the collision with a target electrode. Collision energy causes the rise of potential and causes fission of protein by collision. This can explain that inactivation of AP is increased by the increment in an electrical potential difference and a current. Generation of the product by the corona of the electrostatic atomization deposition of I by 200-300 or more nAs becomes clear with the property of the smell of the ozone in an electrostatic atomization chamber. Disappearance of the thing of the shape of maintaining a high current, after a pump stops, and a torch of visible electrostatic atomization also shows existence of corona discharge under these situations. It became clear that the electrostatic atomization in a high current also made silver plating exfoliate from a capillary tube tip as a result. The capillary tube with an external electrode can explain why AP is inactivated by the low current to higher extent, when corona discharge is maintained easily and electrostatic atomization deposition is carried out from a capillary tube with an external electrode by this rather than a capillary tube with an internal electrode. Since adding AgNO3 of 10-4M to AP solution is not checked at all, it deserves attention that the contamination by Ag ion of the deposit of AP does not bring about inactivation of the deposit of AP from a capillary tube with an external electrode.

These experiments prove that AP makes more the activity save [be / it / under / direct drying / comparing] on the conditions that deposition of electrostatic atomization does not exceed the electrical potential difference of +4.5kV from a capillary tube with an internal electrode, but is carried out with less than 50 nA of currents regardless of the mechanism of inactivation of the electrostatic atomization deposition under the high voltage and a high current. On these conditions, the damage factor mentioned before is not generated at all, but it is thought that only a desiccation process is the factor of inactivation left behind only only one. When processed by freeze drying, it is described in written form well that much protein loses the activity, and some in it are completely inactivated by freeze drying or desiccation of a room temperature (1992 besides 1987 besides Crowe, and Gibson). It is also known well that a disaccharide has the function to protect protein in desiccation (1992 besides Gibson). The data shown in this drawing 22 show that AP is similarly protected from inactivation by desiccation by both cane sugar and trehalose. It is enough to save the activity of AP 100% if this disaccharide is added 50% (w/w). It is shown that the curve of the drawing 18 A top protects the activity of AP in desiccation, and the cane sugar which are the same matter protect it well similarly in deposition of electrostatic atomization. If electrostatic atomization deposition makes concentration (50%w/w) of cane sugar the same on the conditions of carrying out from a capillary tube with an internal electrode with a small current, 100% of the activity of dry AP will be protected, and existence of these cane sugar will raise recovery of the activity of AP of the enzyme deposited in electrostatic atomization to 100%. These results point to desiccation being the factor of main damage under the conditions of such electrostatic atomization. In the situation of humidity with the low result of drawing 23 , there is little damage which gives the quick drying in the gas phase of the drop generated by electrostatic atomization to the activity of AP rather than low-speed desiccation (drawing 22 shows reduction 45%) of the solution on a front face (30% reduction). However, this enzyme receives greater damage, when electrostatic atomization deposition is carried out at the humidity exceeding 60%. Probably, the cycle of the multiple times of /desiccation which become wet is presumed to be the cause, and the thing in accordance with descent of a minute drop completely dried in the stroke to a base on this condition does not have this drop. That is, when deposition of electrostatic atomization is carried out on ****** conditions under existence of a protector, the functional activity of AP can be completely saved in deposition of the electrostatic atomization to a metal electrode.

Please fully explain this invention and this contractor needs to understand it as what can carry out this invention on an equivalent parameter, concentration, and conditions in the large range on the conditions which do not separate from that it is not the experiment with unsuitable **, the range of this invention, and the meaning.

Although this invention has been explained about a concrete suitable example, please understand that many deformation is possible for this invention. Although this application separates from the publication of this specification also including what kind of modification which generally follows in the principle of this

invention, an application, or application, it contains what suits the summary which whether it is known explained previously on these specifications which were used commonly and indicated by the claim in the technical field to which this invention belongs.
It was announced officially or all the bibliographies stated on these specifications contain the patent application of the patent application of a periodical or an epitome, the U.S. equivalent to this, and a foreign country, the U.S. where patent assessment was carried out, and a foreign country, and other bibliographies.
All the parts that these referred to on these specifications including all data, a table, drawing, and the sentence as which it is indicated by quoted reference are included. Furthermore, all the contents of the bibliography quoted in such bibliographies are also altogether contained as bibliography.
The reference about the step of a known approach, the step of the conventional approach, a known approach, or the conventional approach does not admit that the summary of this invention, explanation, or an example is what is indicated, taught and suggested in the technical field concerned.
without it clarifies the general property of this invention enough and leaves not the operation that is not appropriate but the general concept of this invention by applying the conventional technique (the contents of the reference which this specification quotes being included) so that others can carry out the concrete above-mentioned explanation about a suitable example -- a specific suitable example -- like -- various application -- easy -- modification -- and -- or it suits. Therefore, such adaptation and modification are due to suggestion and instruction which had the intention of being the range equal in the indicated suitable example, and the range of an approach, and explained it on these specifications. The phrase of this specification and a technical term are for the purpose of explanation, and are not limited by this. Such a phrase in this specification and a technical term are interpreted by this contractor in consideration of suggestion of this specification, and instruction combining the knowledge of those who have the general technique of the technique concerned.

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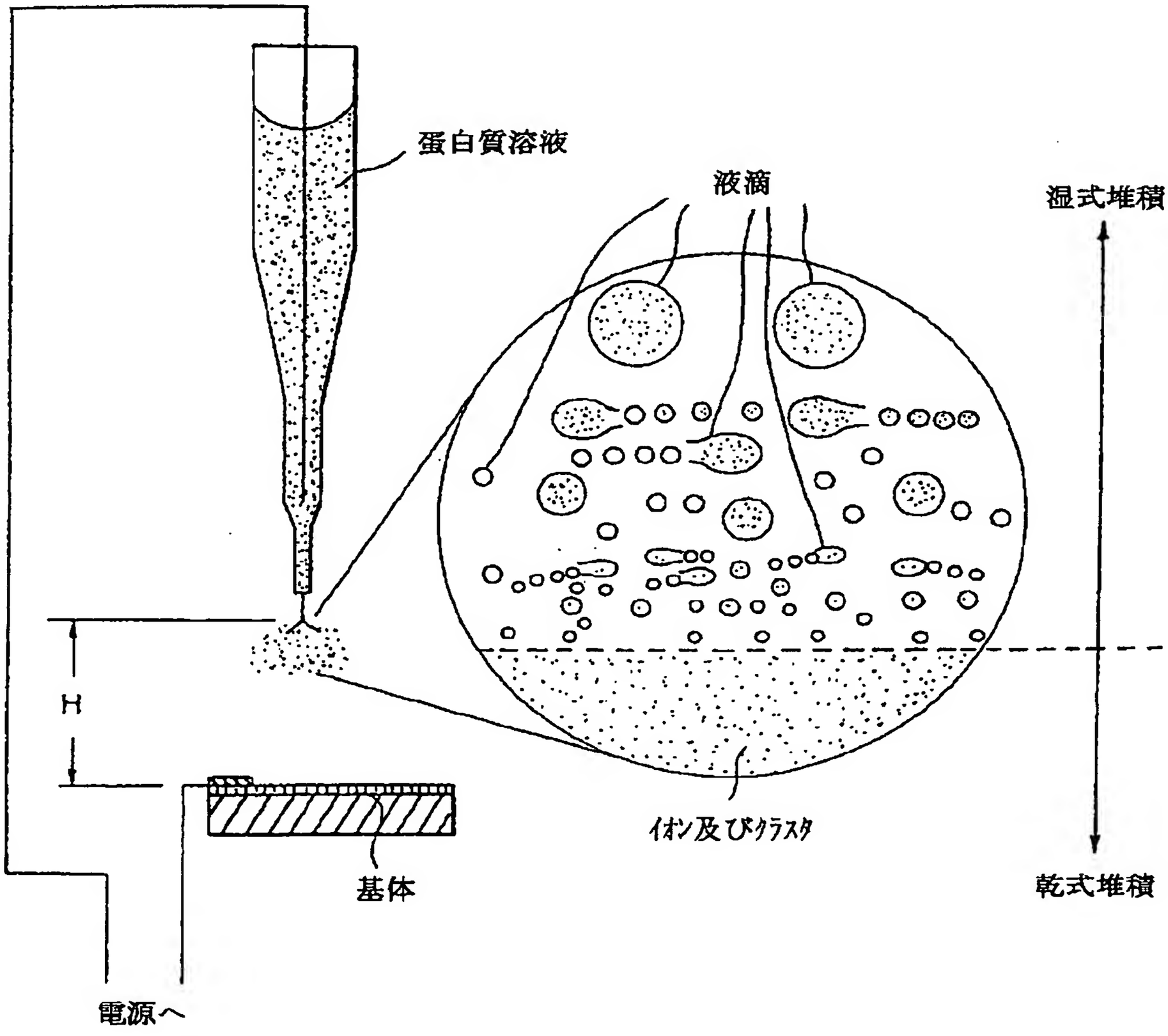
[Translation done.]

DRAWINGS

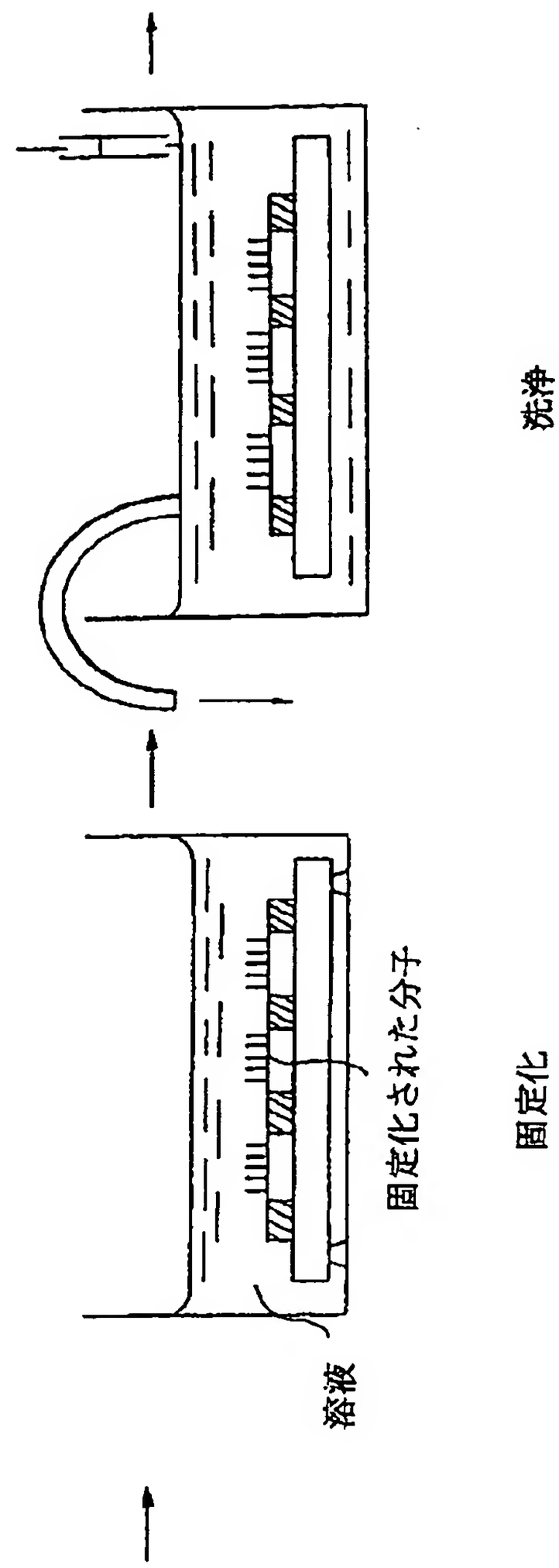
[Drawing 1]

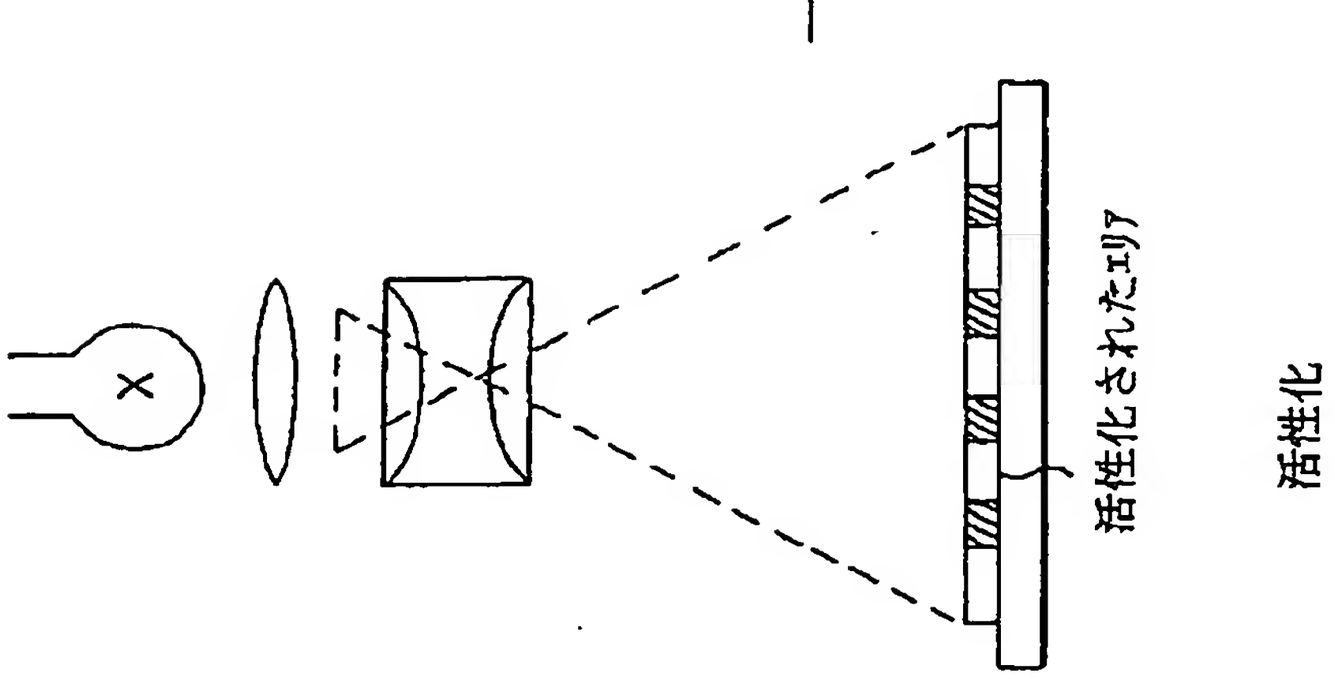
FIG. 1



[Drawing 2]

FIG. 2





[Drawing 3]

FIG. 3A

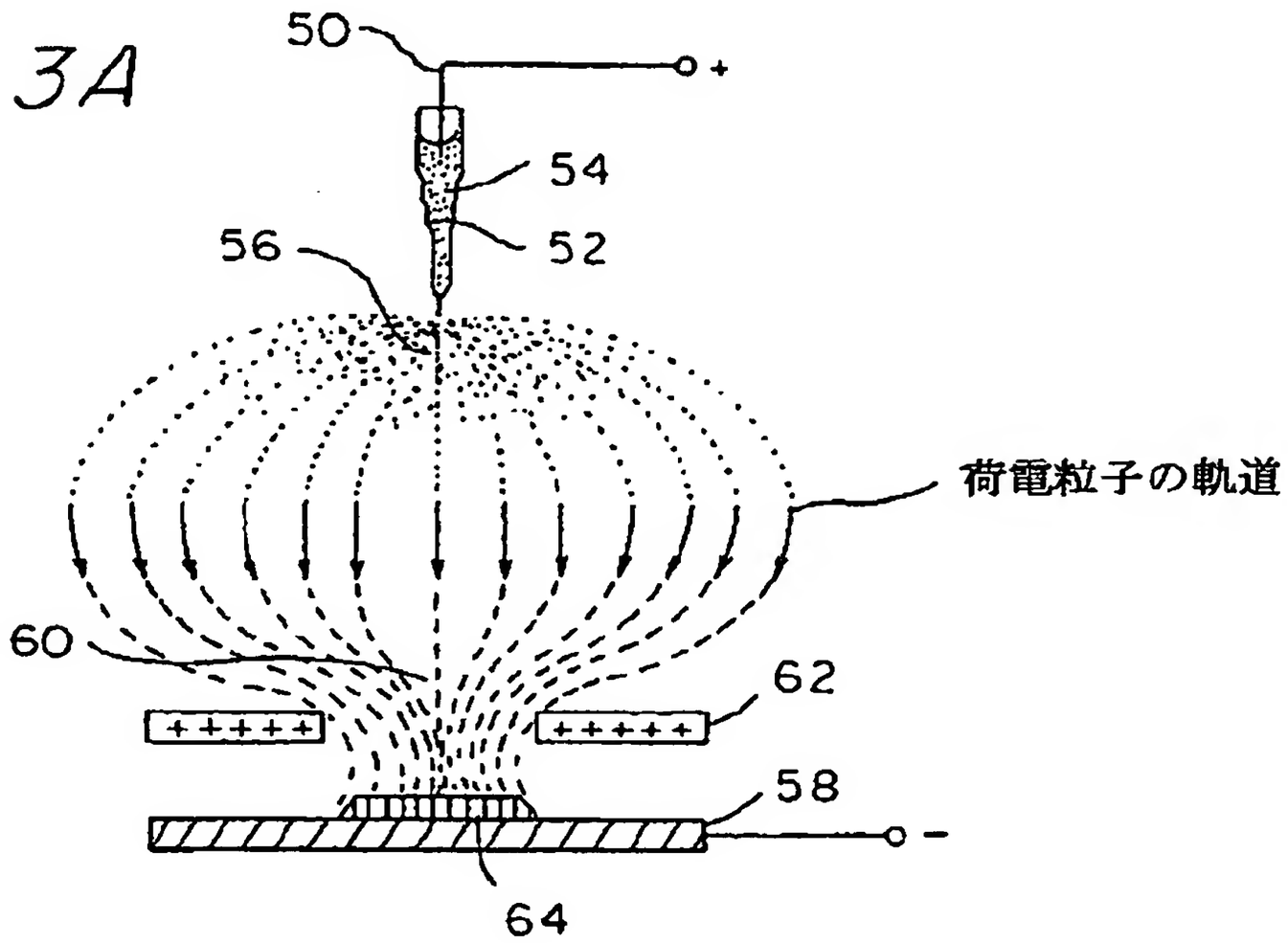
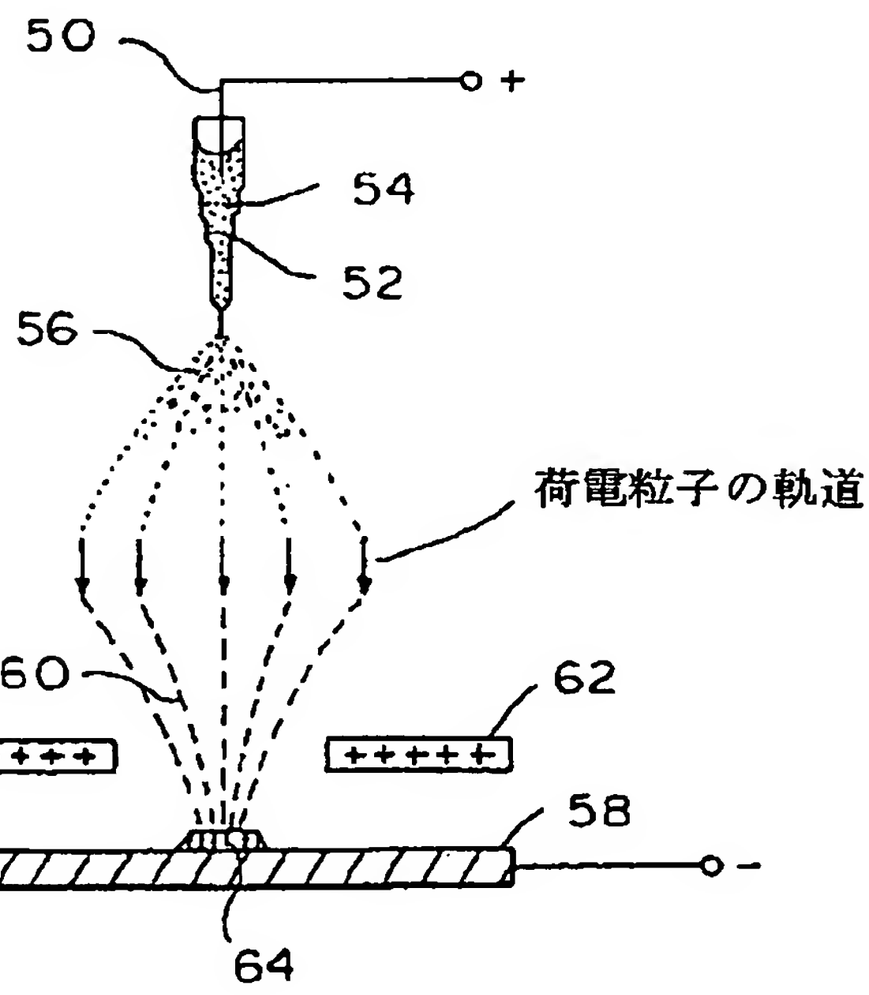


FIG. 3B



[Drawing 4]

FIG. 4A

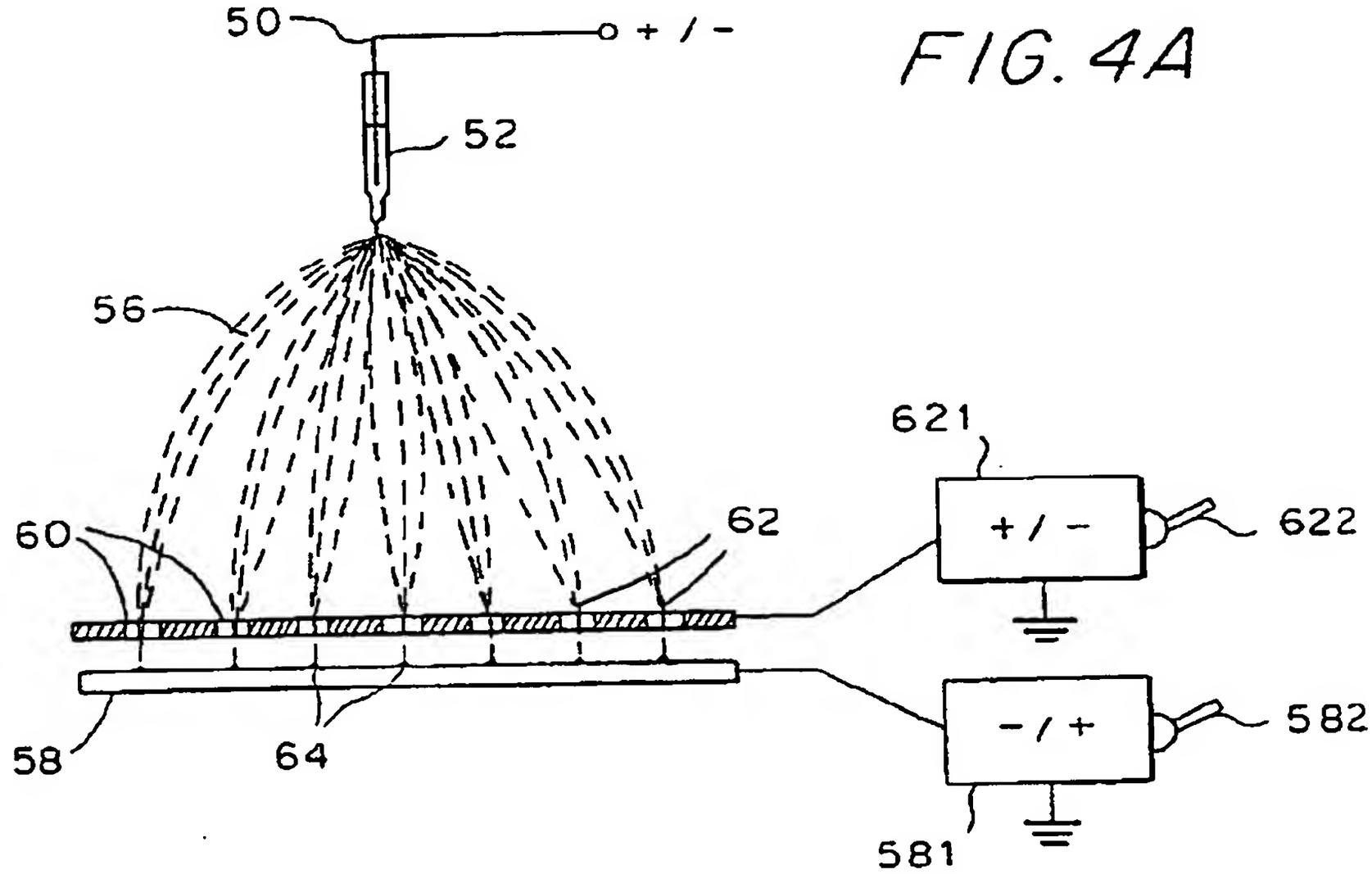


FIG. 4B

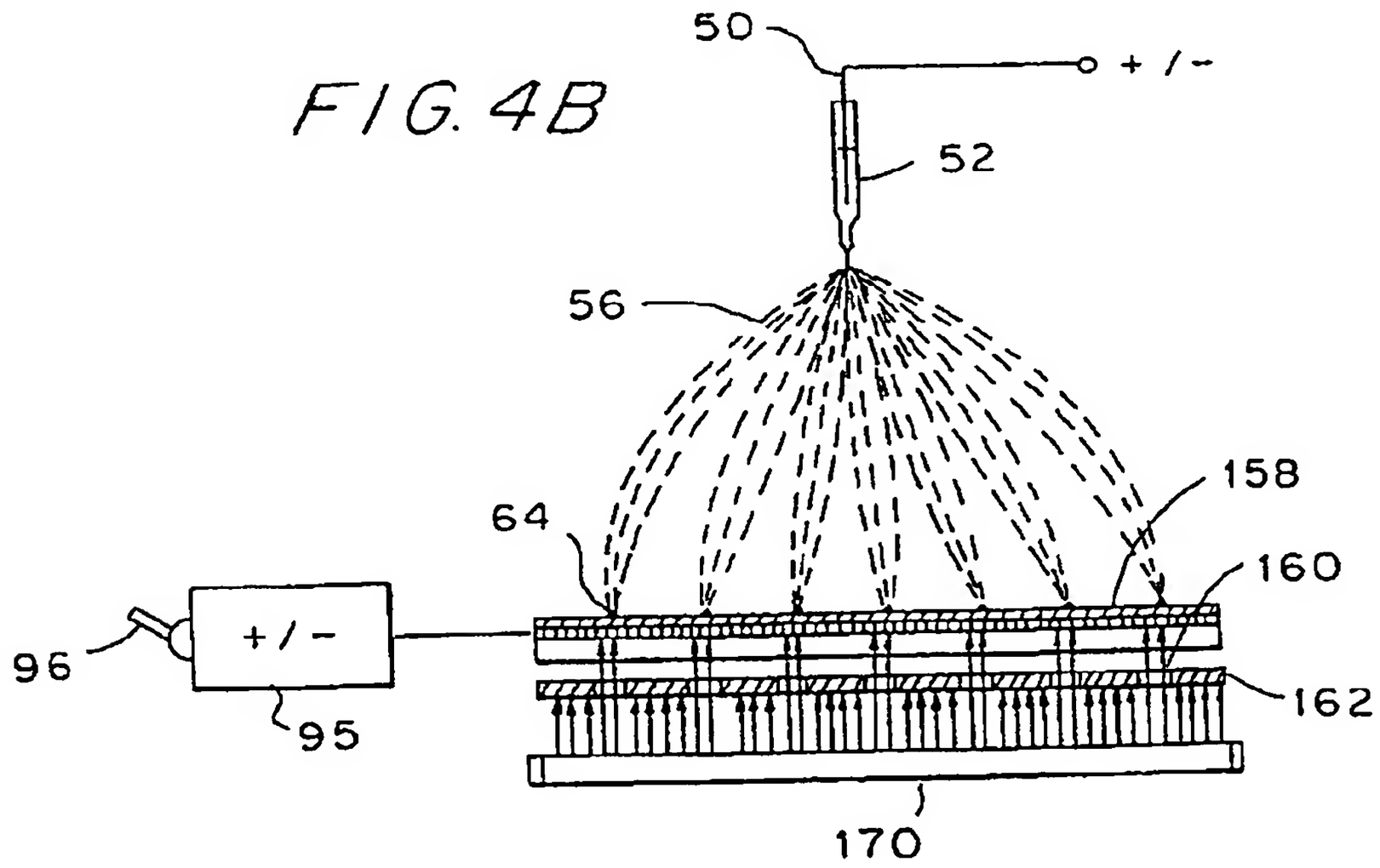
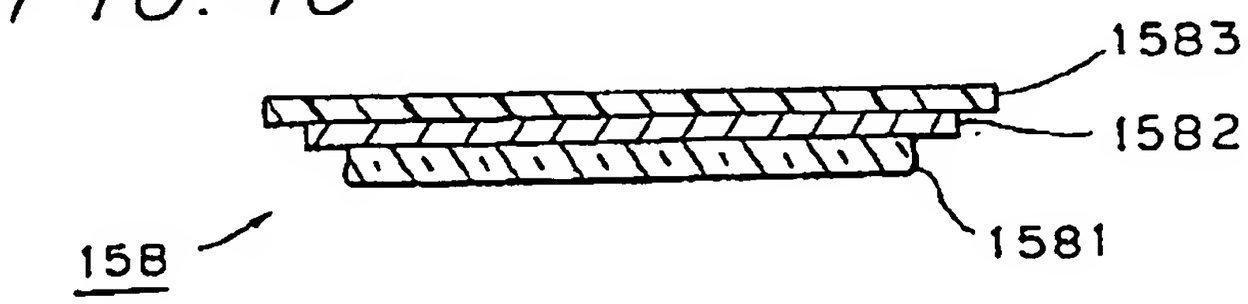


FIG. 4C



[Drawing 5]

FIG. 5A

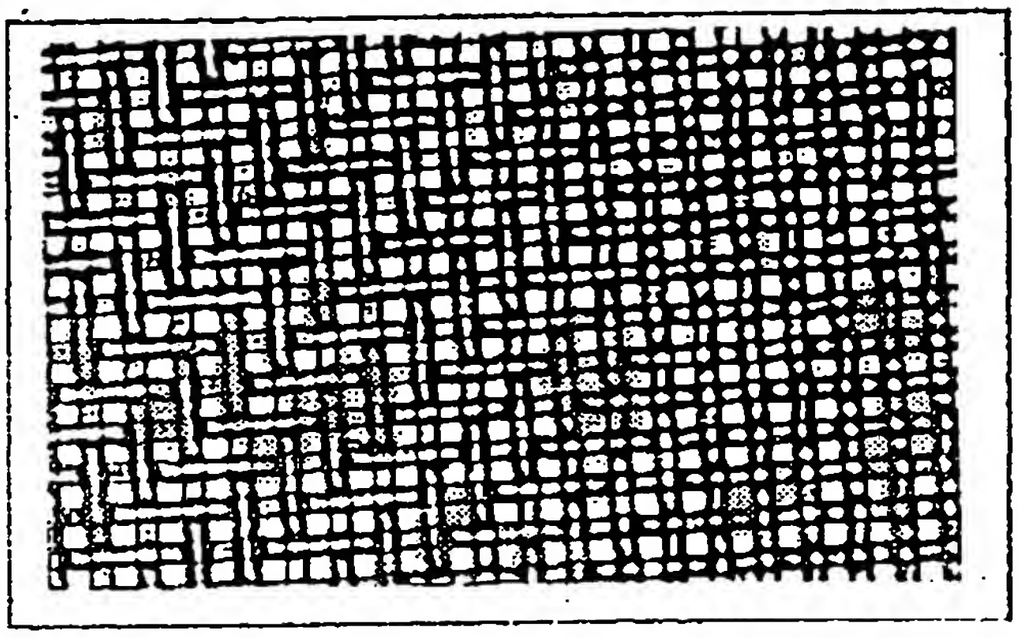


FIG. 5B

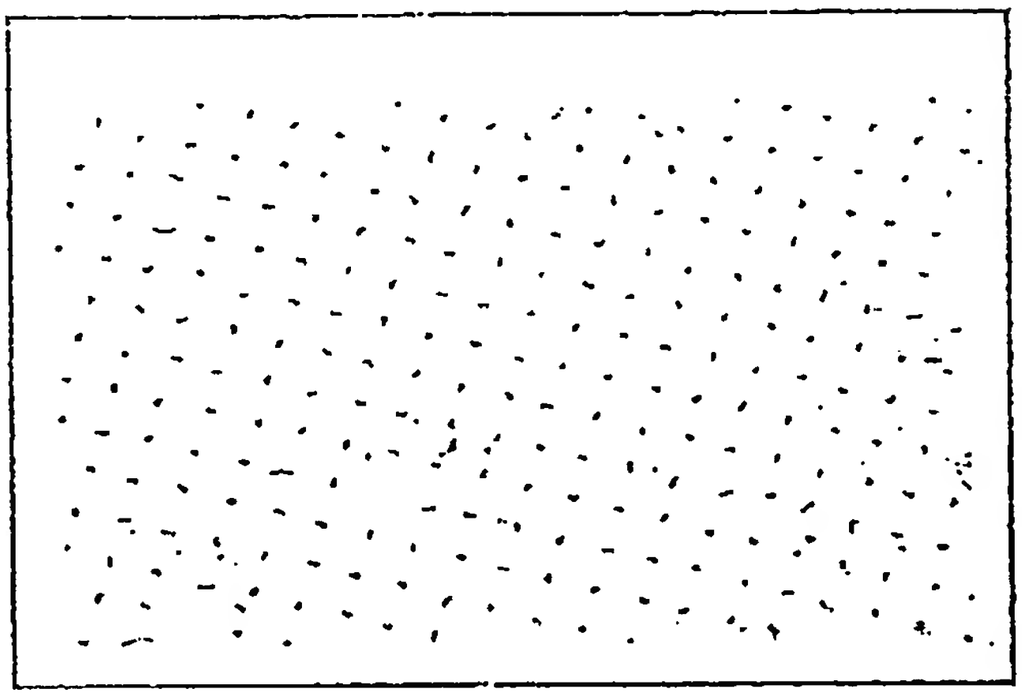
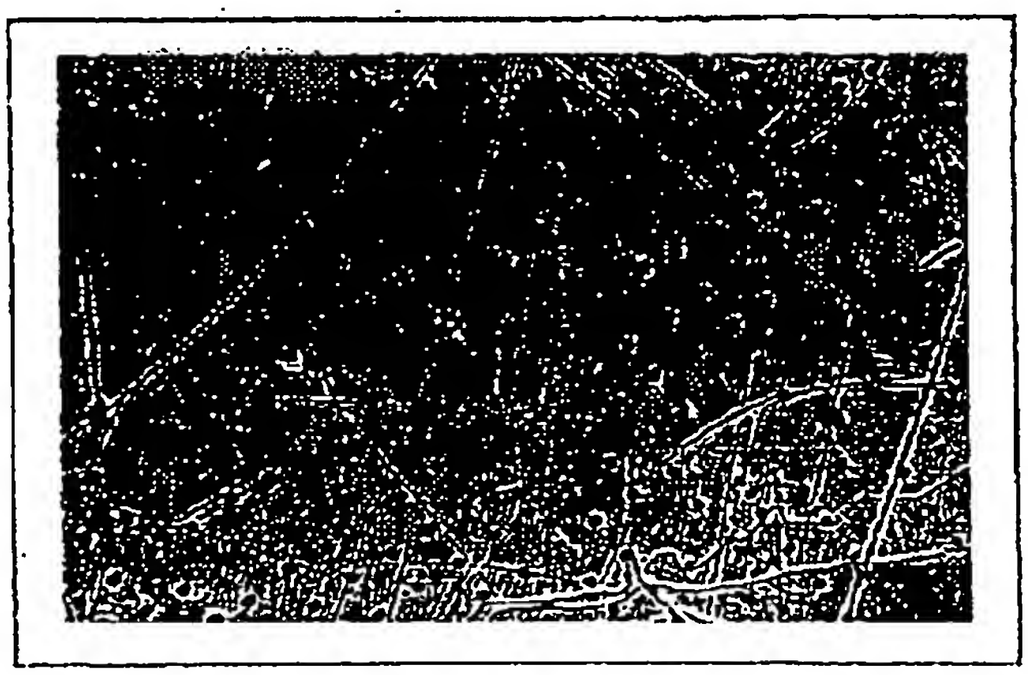
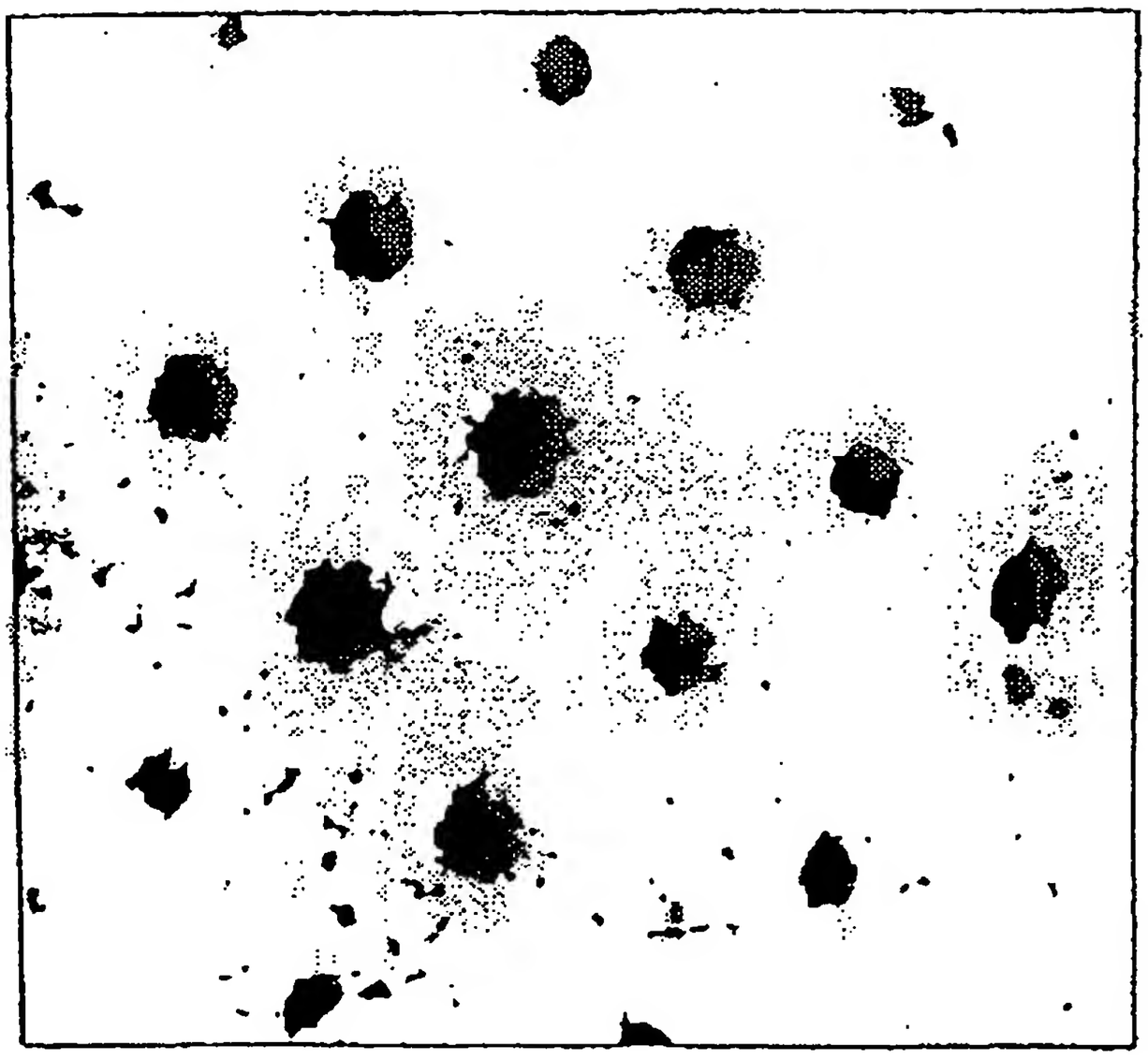


FIG. 5C



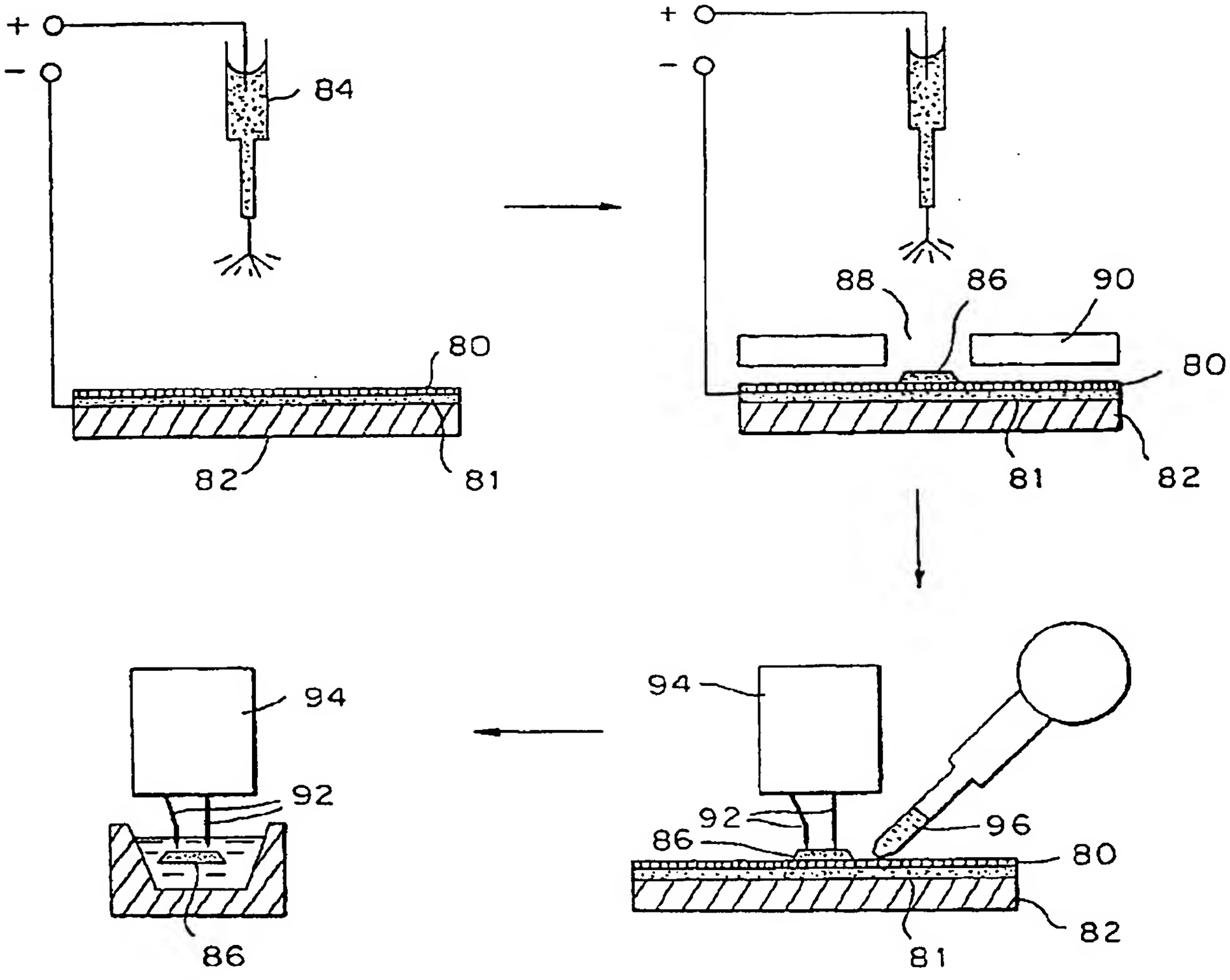
[Drawing 5]

FIG. 5D



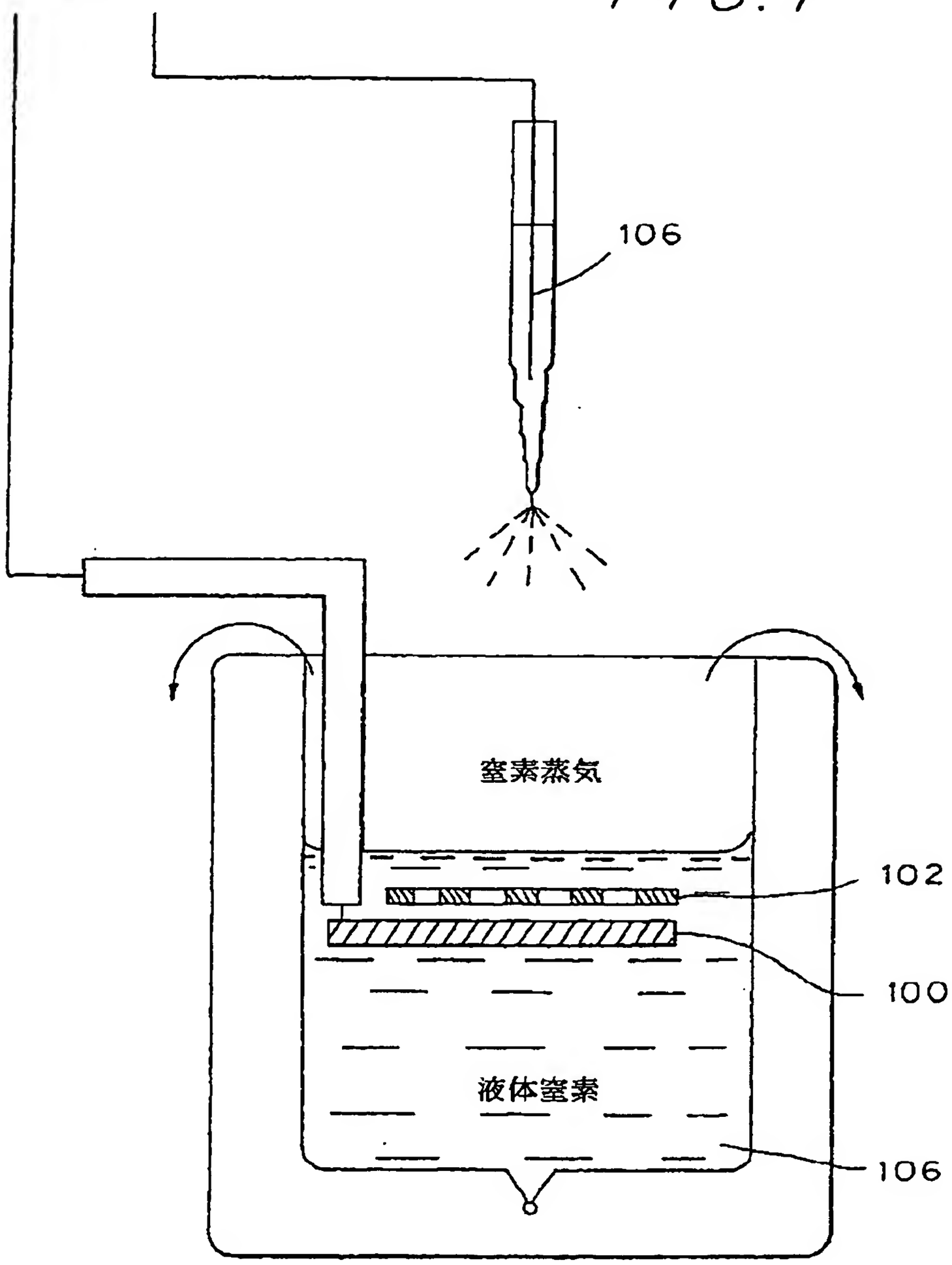
[Drawing 6]

FIG. 6



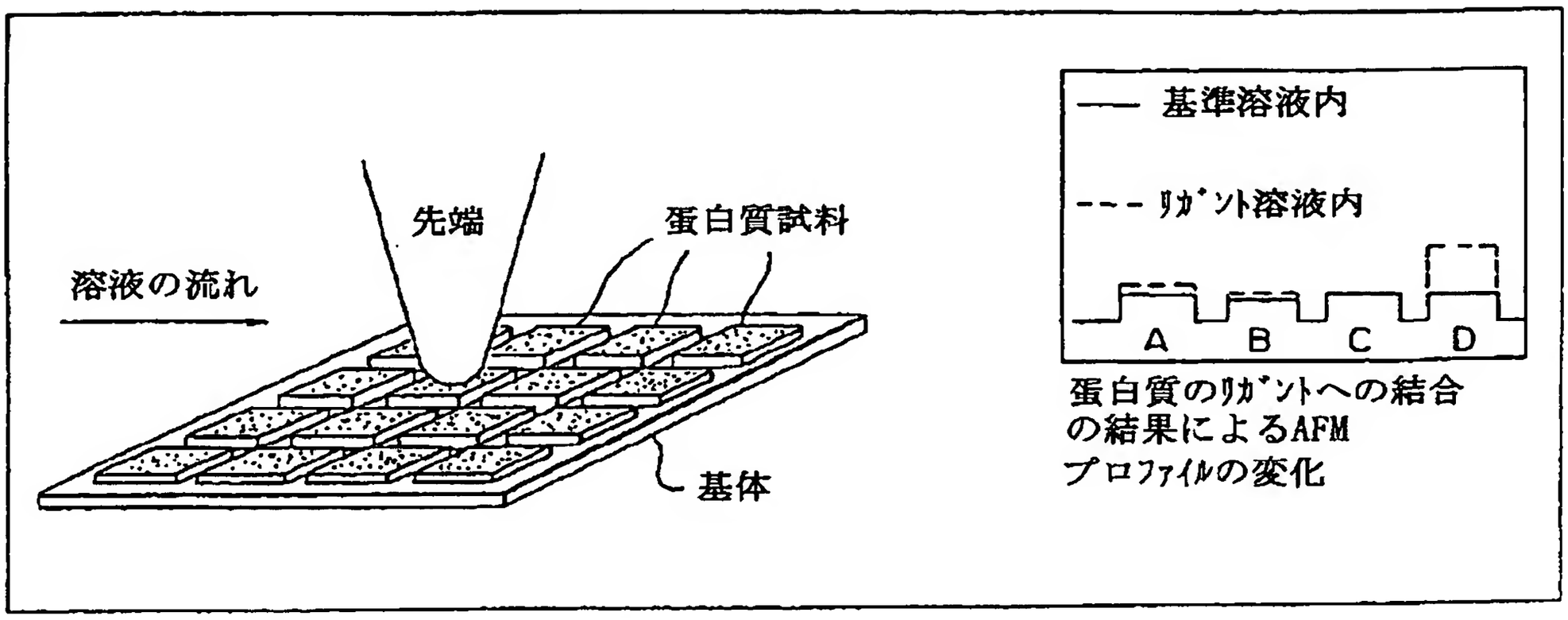
[Drawing 7]

FIG. 7



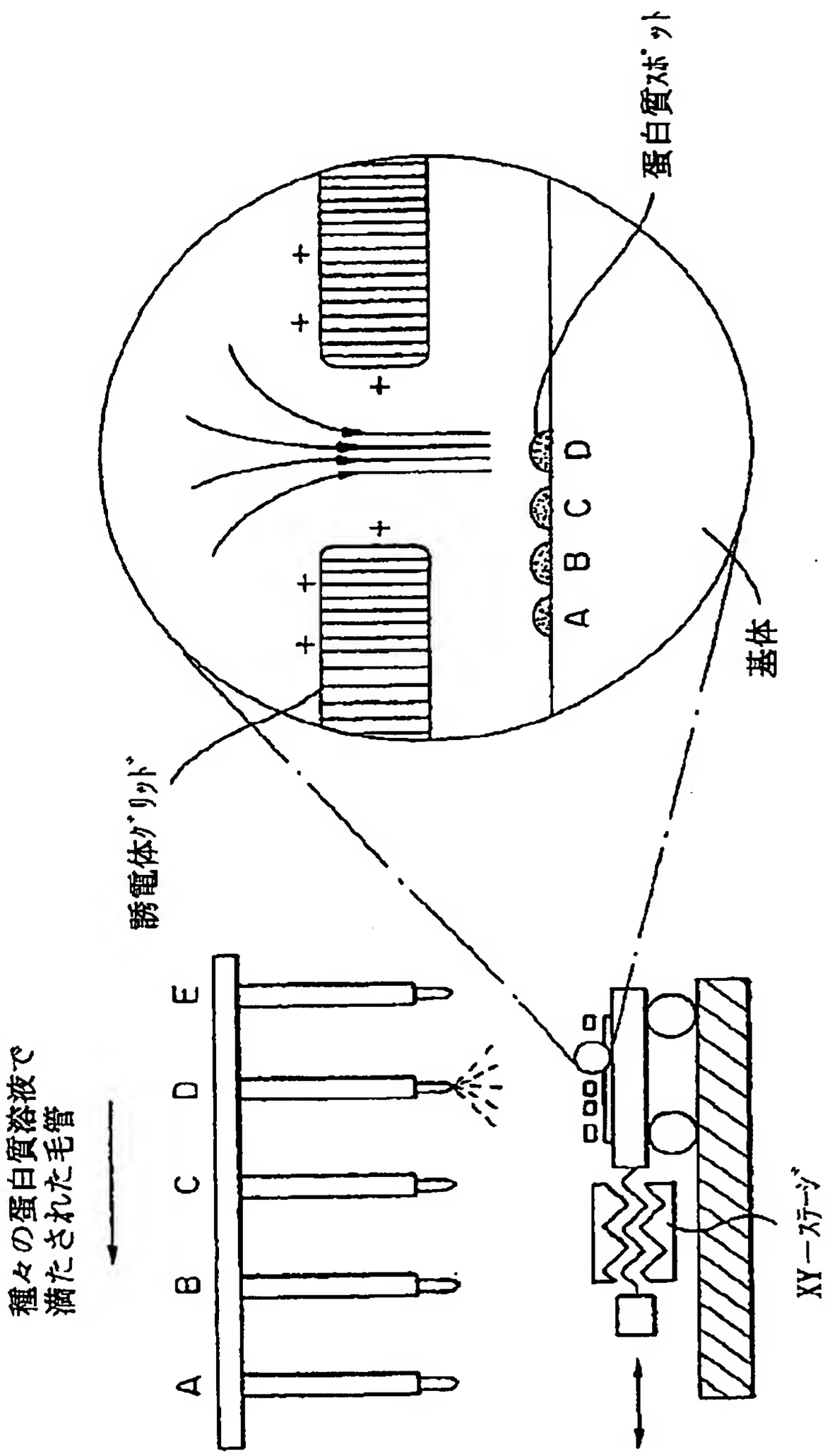
[Drawing 8]

FIG. 8



[Drawing 9]

FIG. 9



[Drawing 10]

FIG.10A

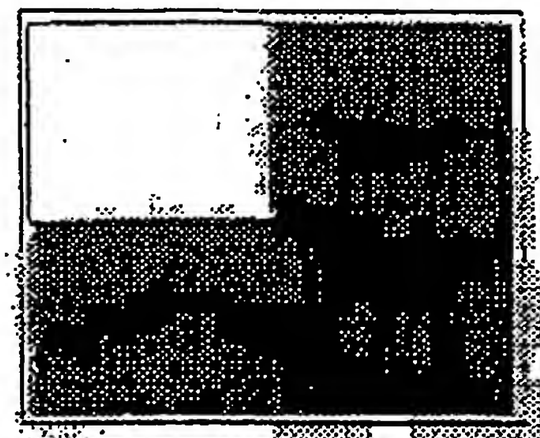


FIG.10B

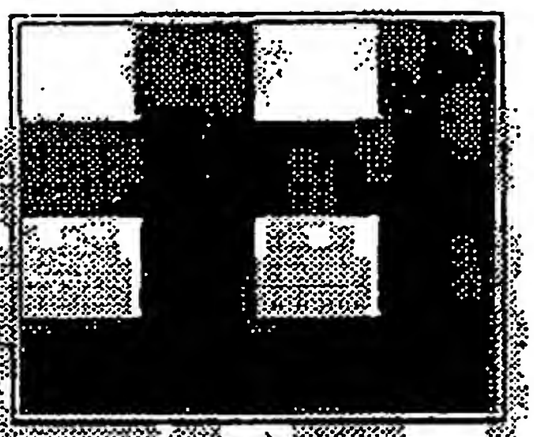


FIG.10C

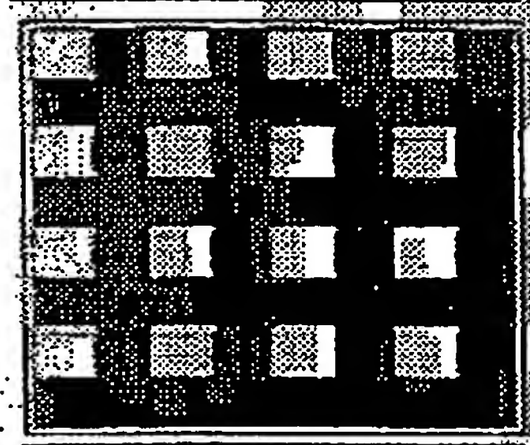


FIG.10D

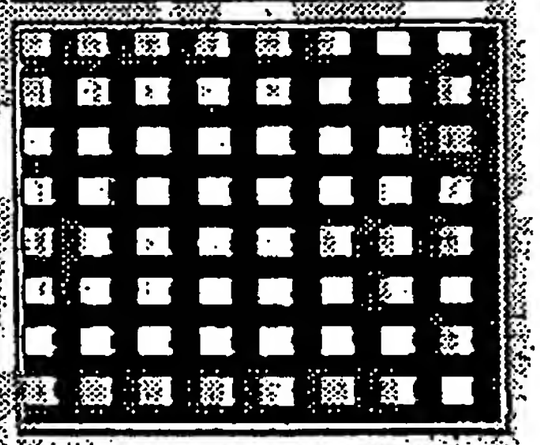
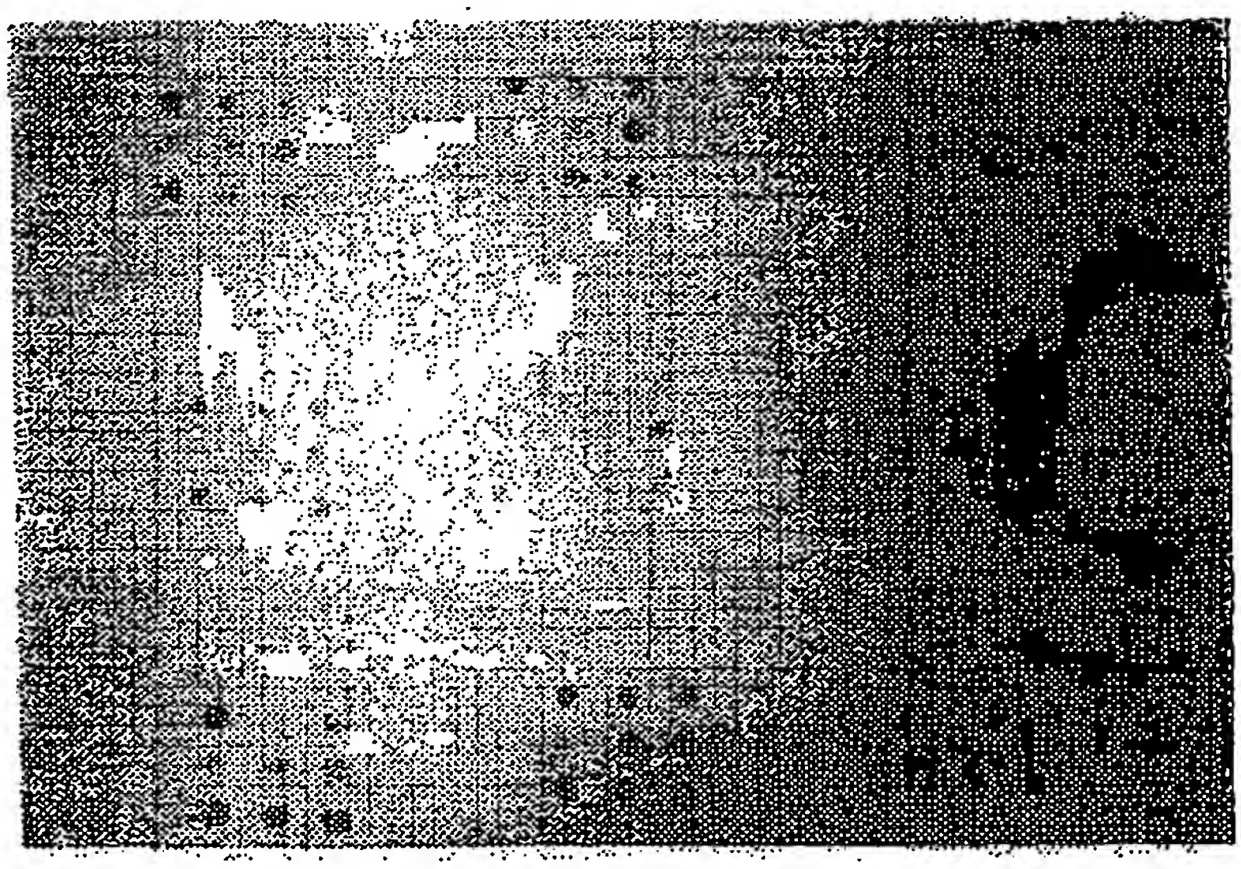


FIG.10E

FIG.10F

[Drawing 11]

FIG. 11



[Drawing 12]

FIG. 12A

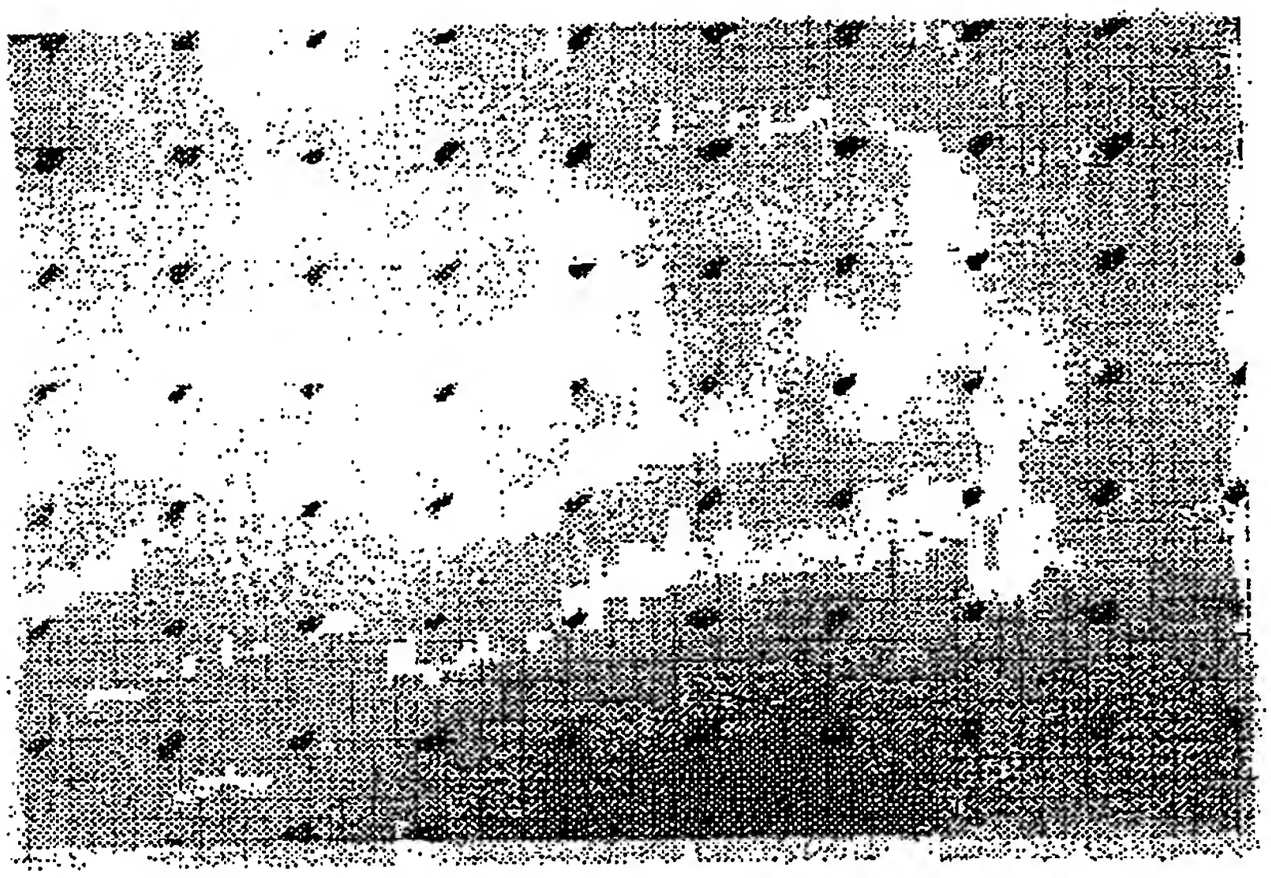
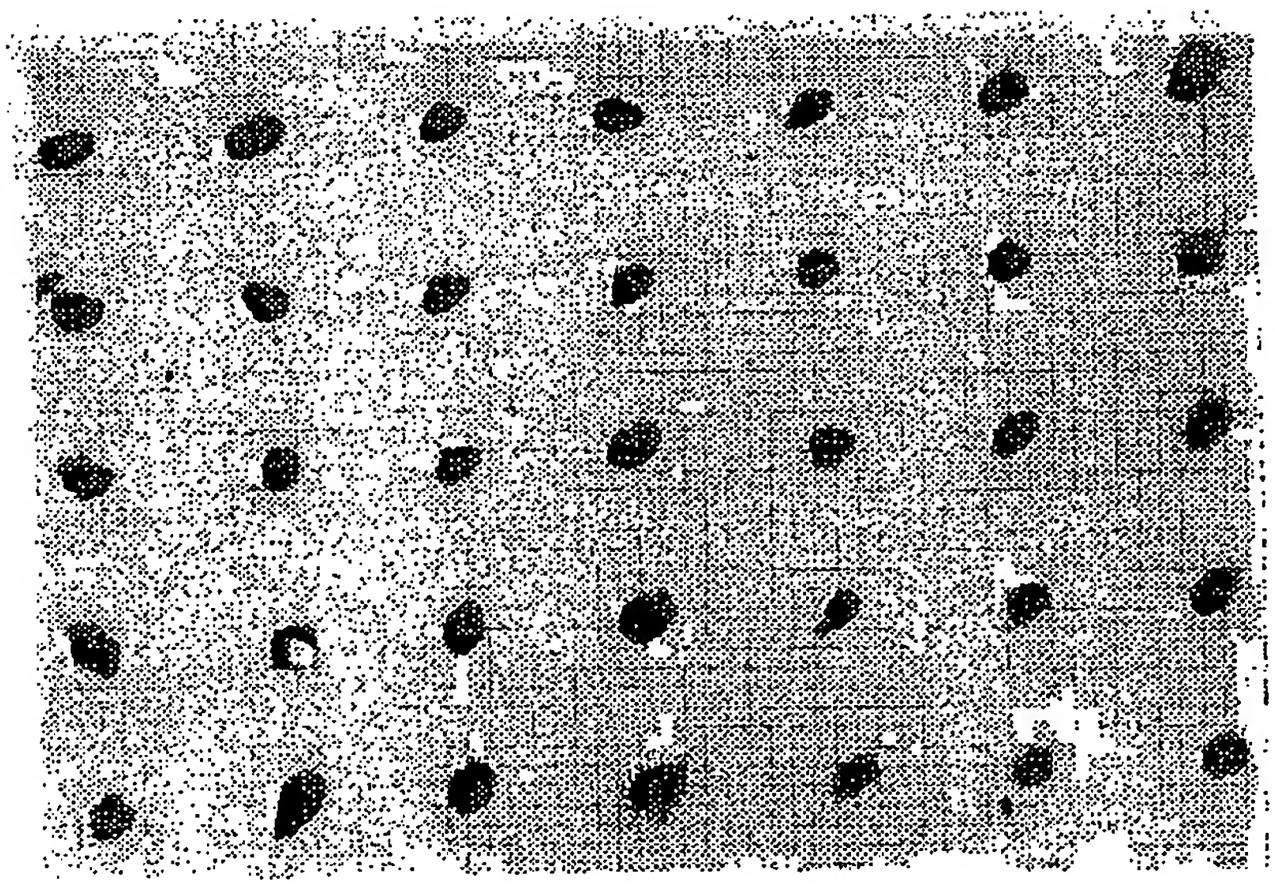
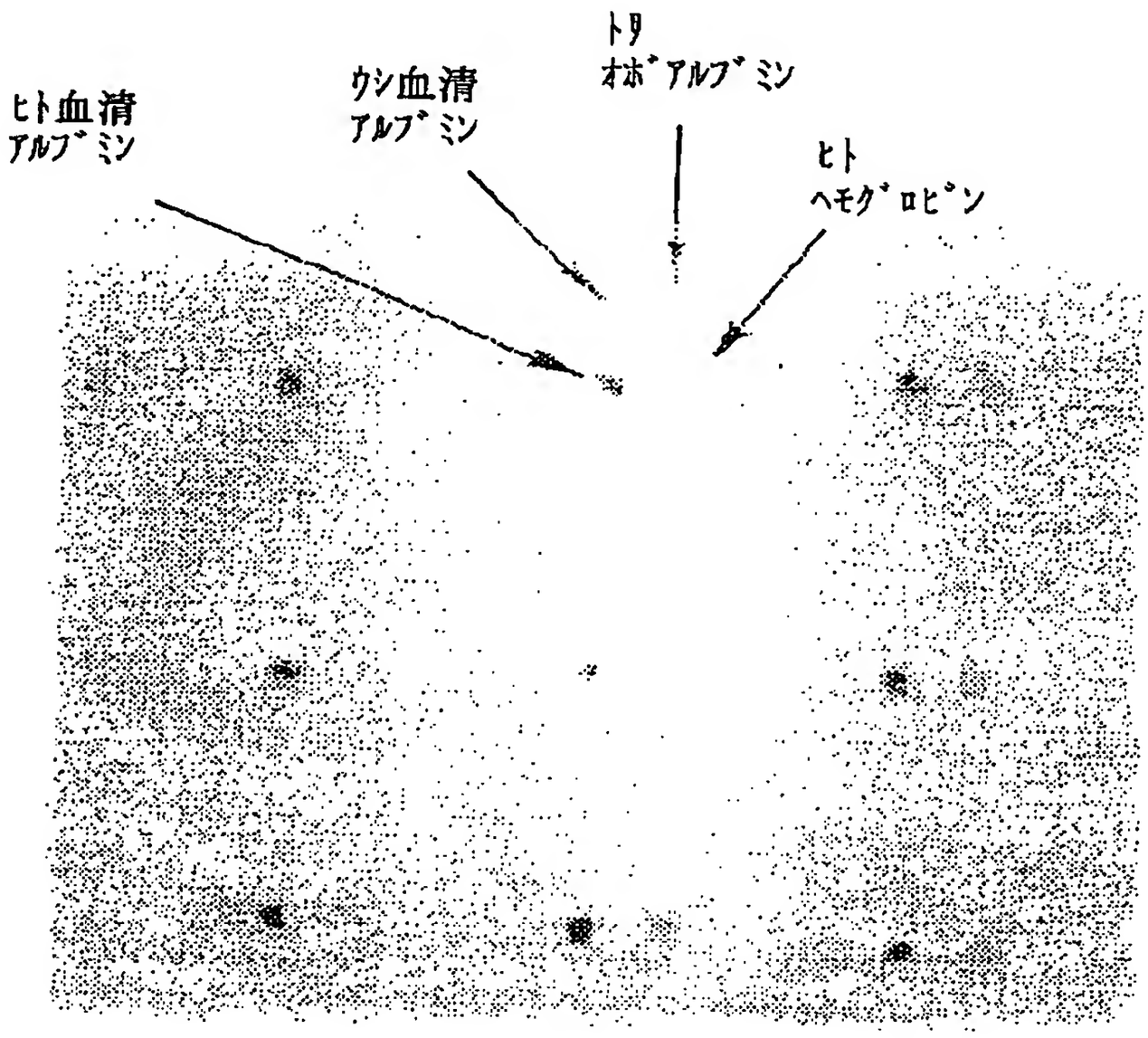


FIG. 12B



[Drawing 13]

FIG. 13



[Drawing 14]

FIG. 14A

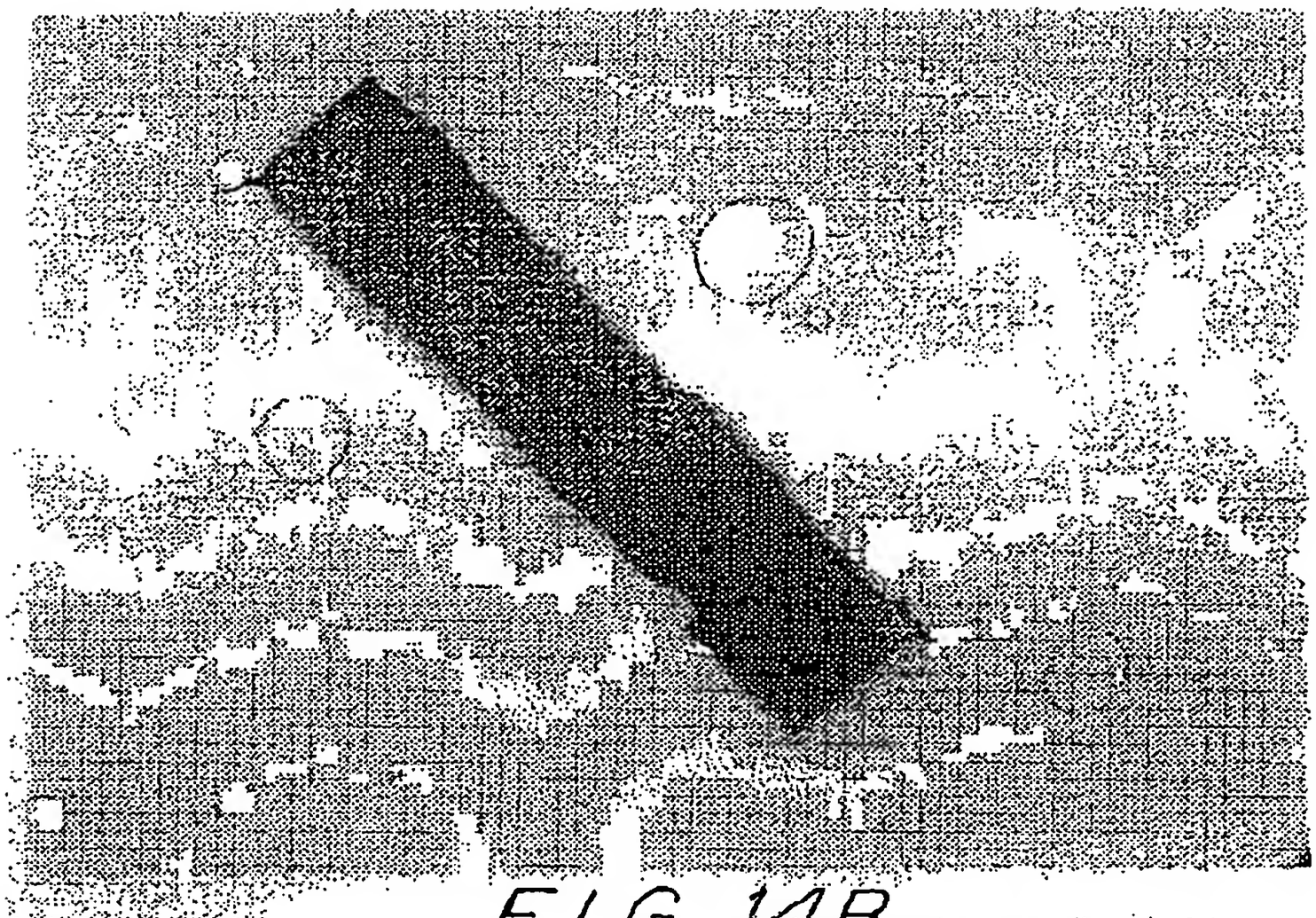
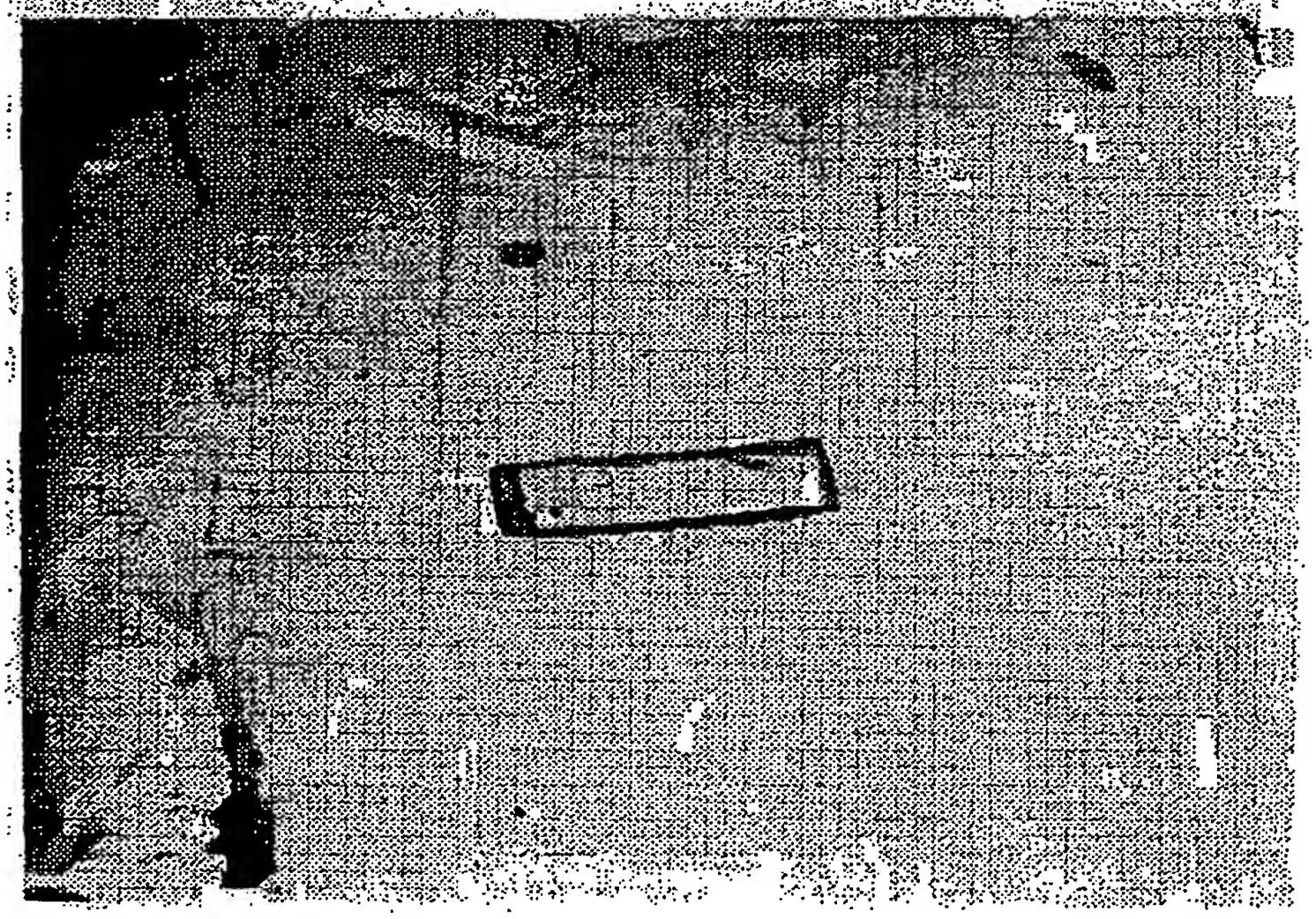


FIG. 14B



[Drawing 15]

FIG. 15A

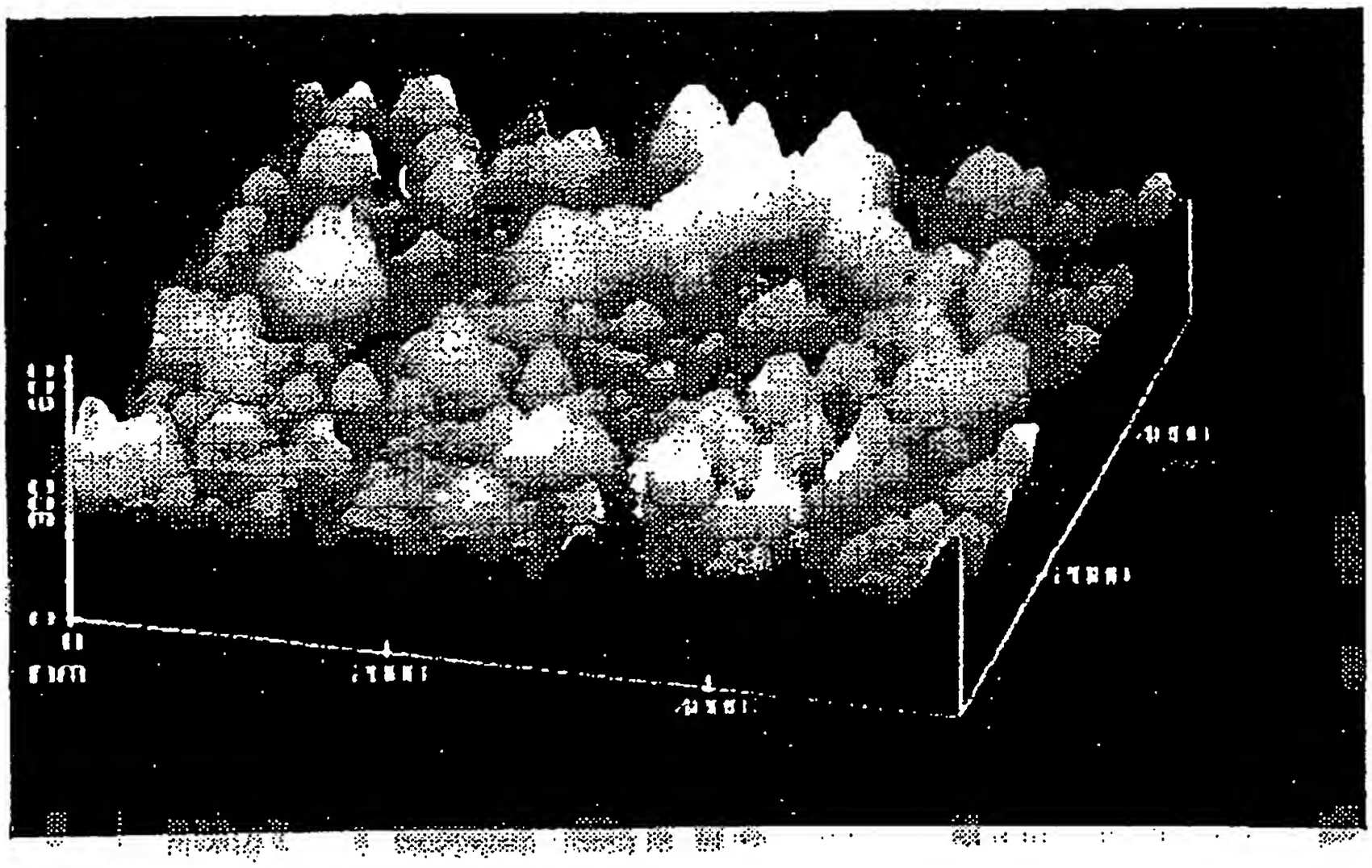
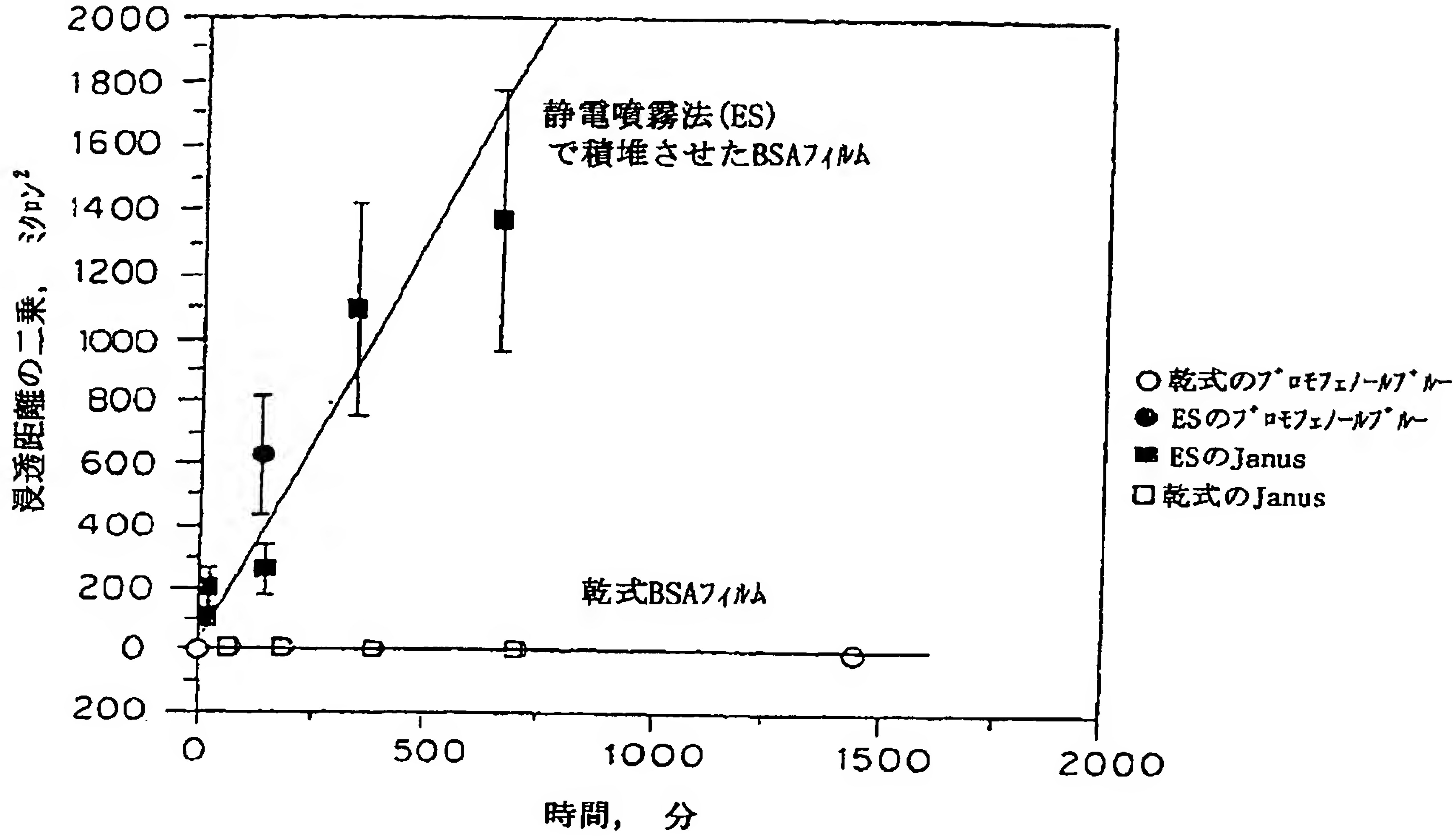


FIG. 15B

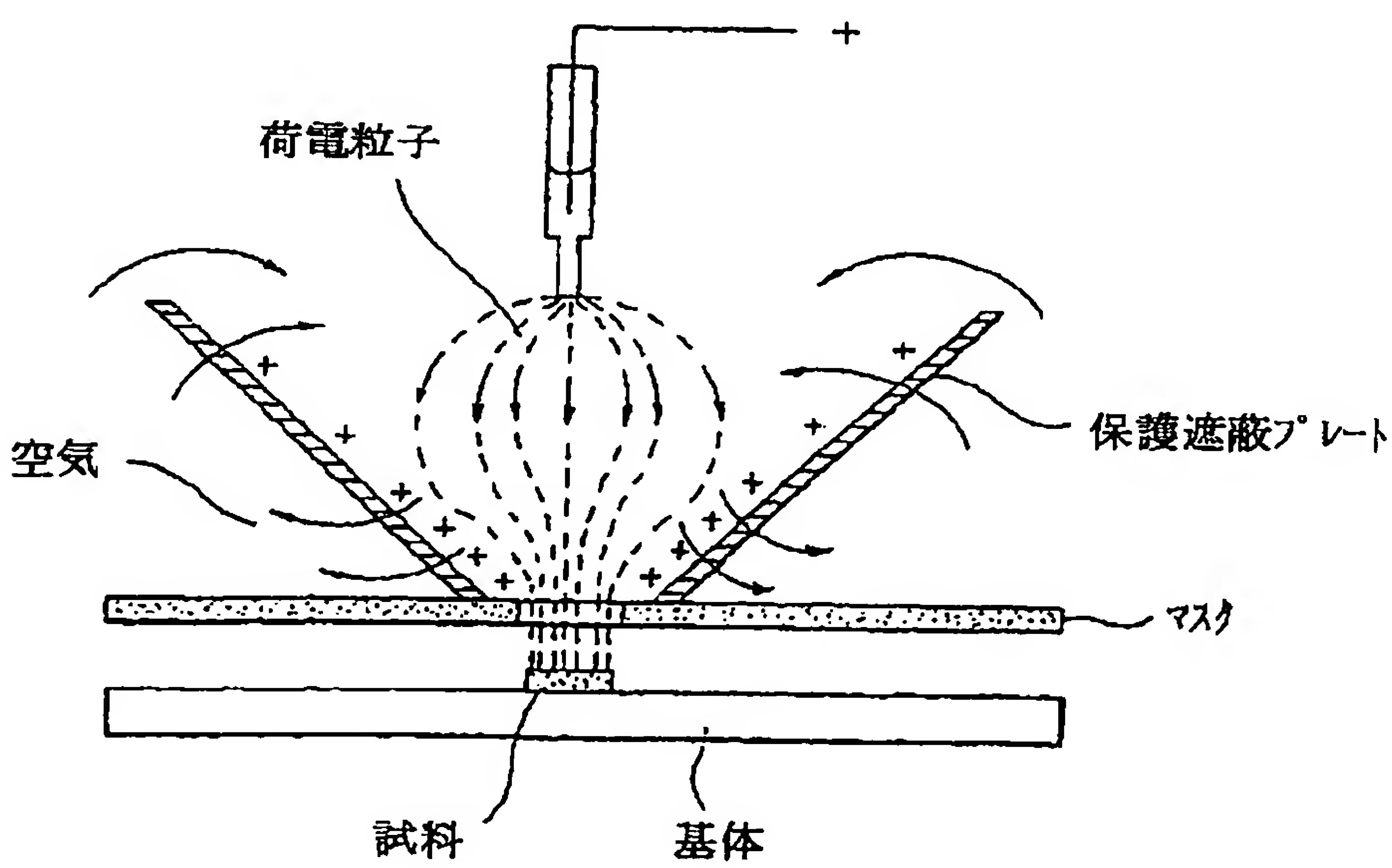
[Drawing 15]

FIG. 15C



[Drawing 16]

FIG. 16A



[Drawing 16]

FIG. 16B

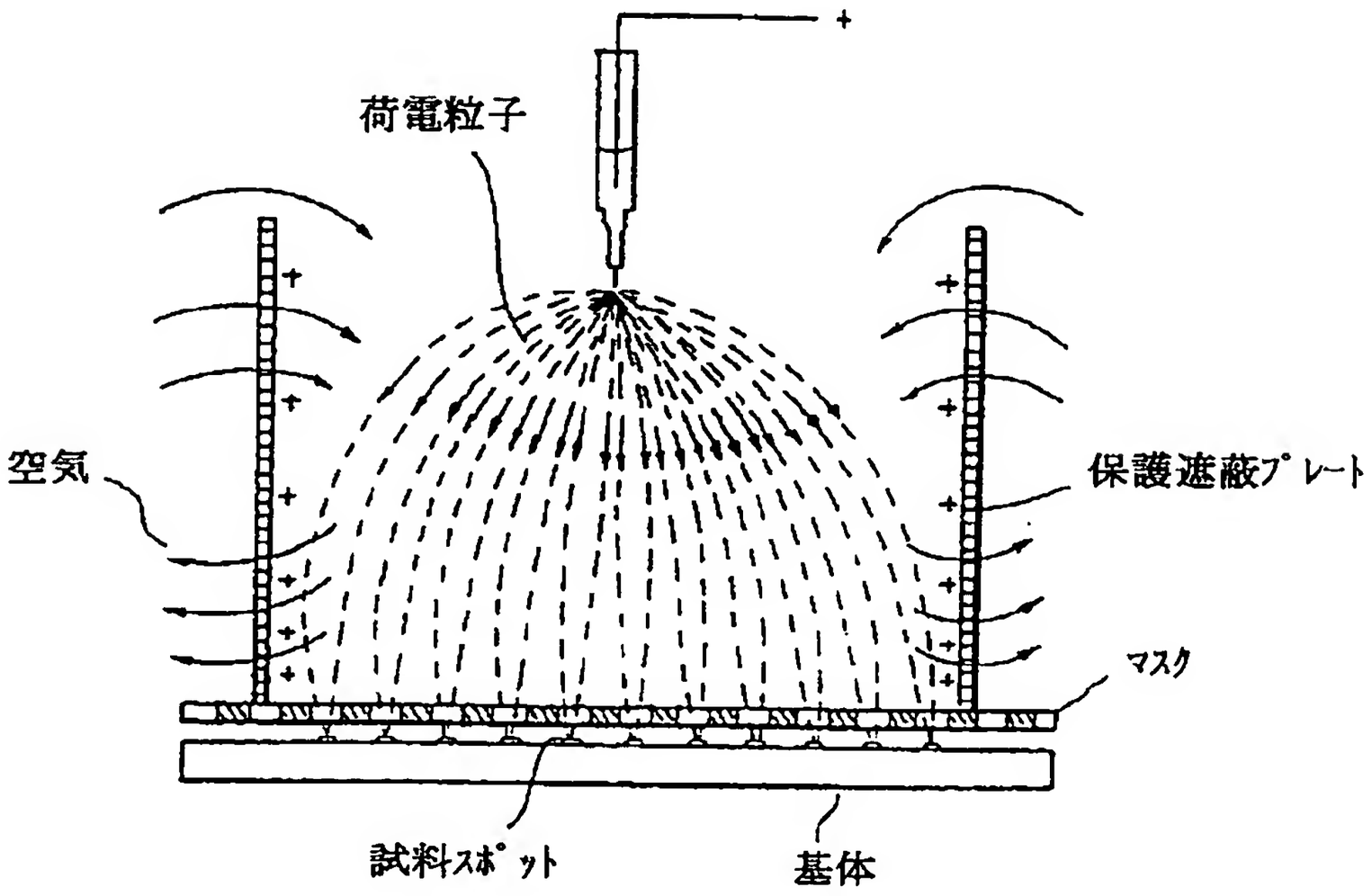
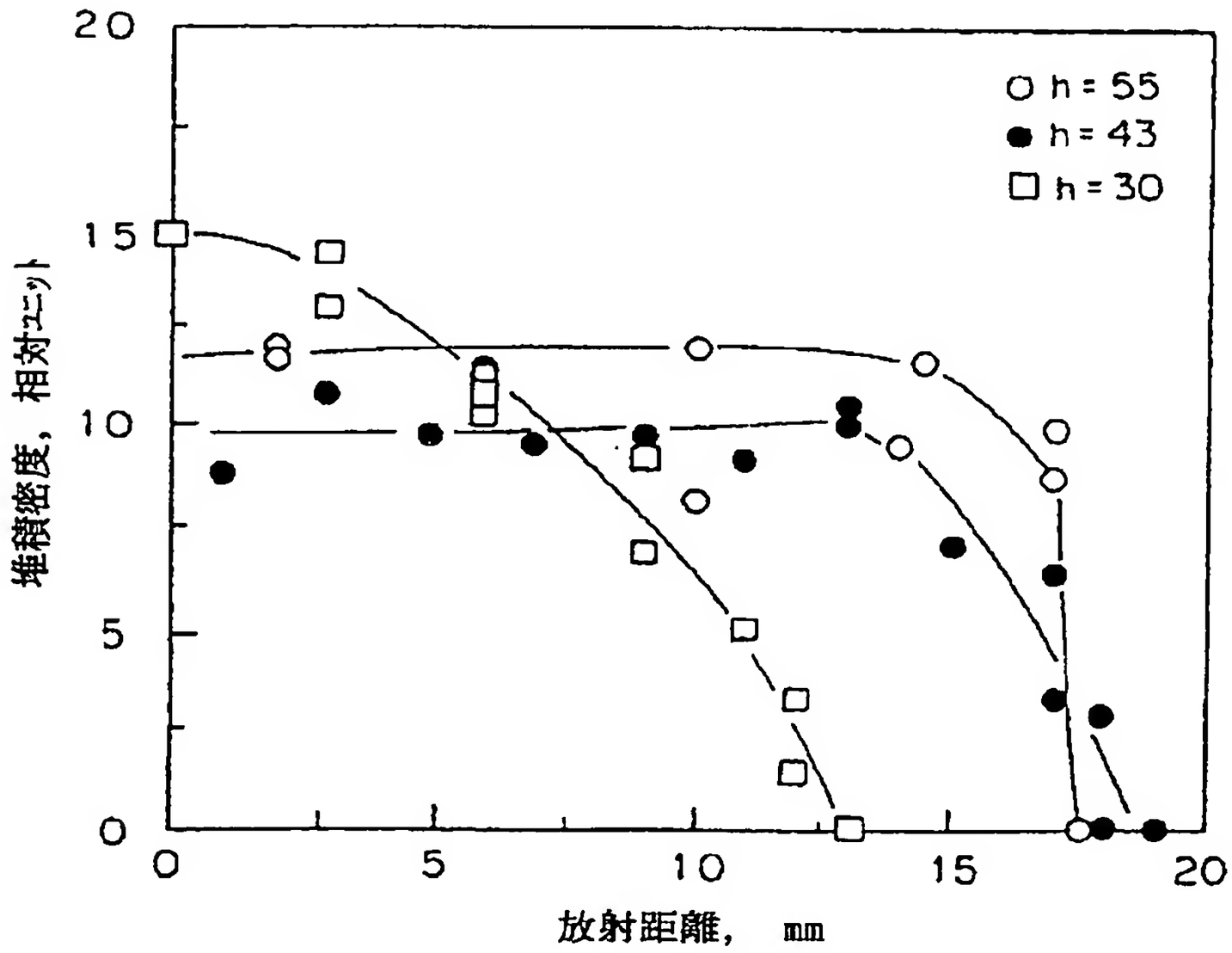
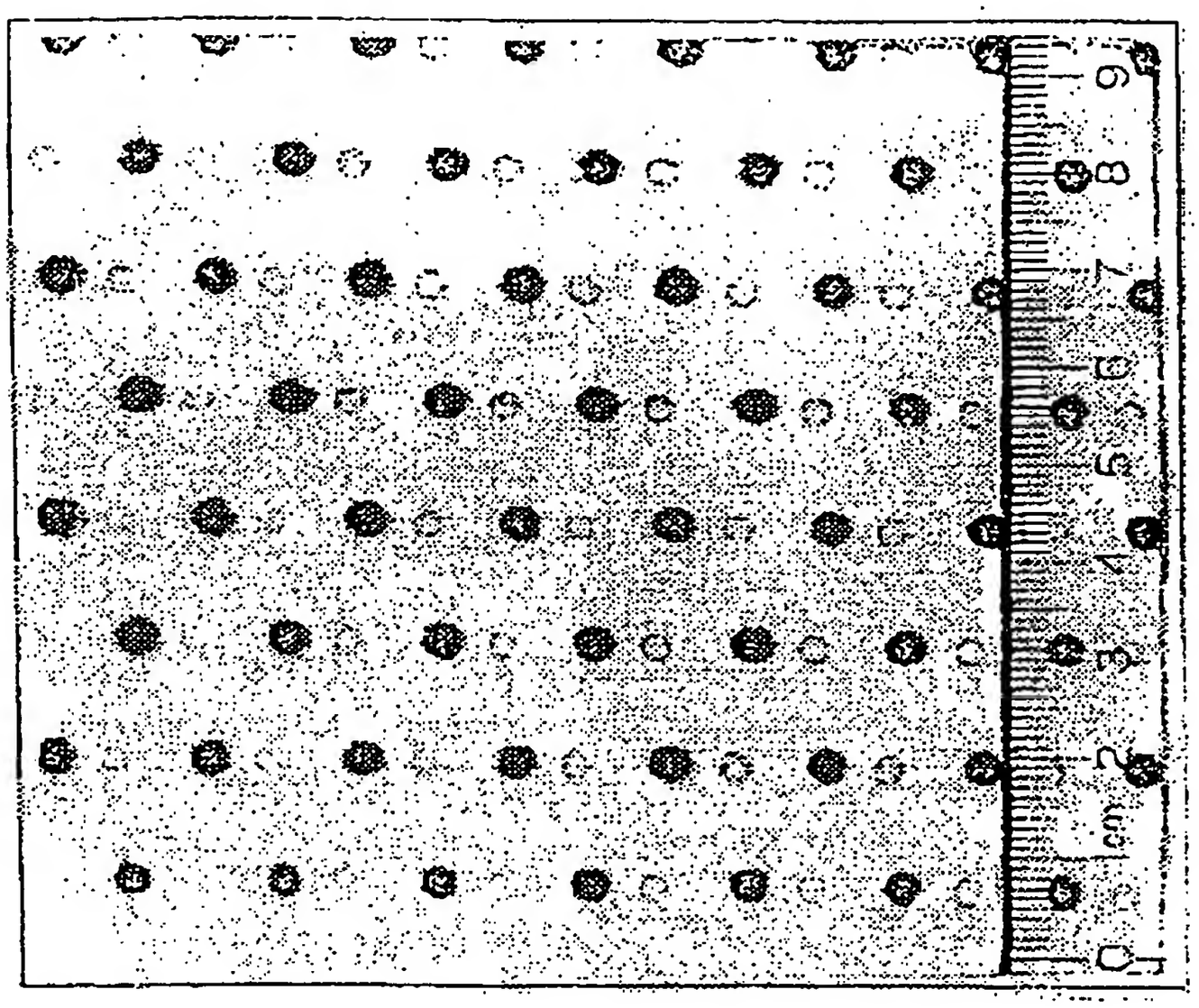


FIG. 16C



[Drawing 17]

FIG. 17



[Drawing 18]

FIG. 18A

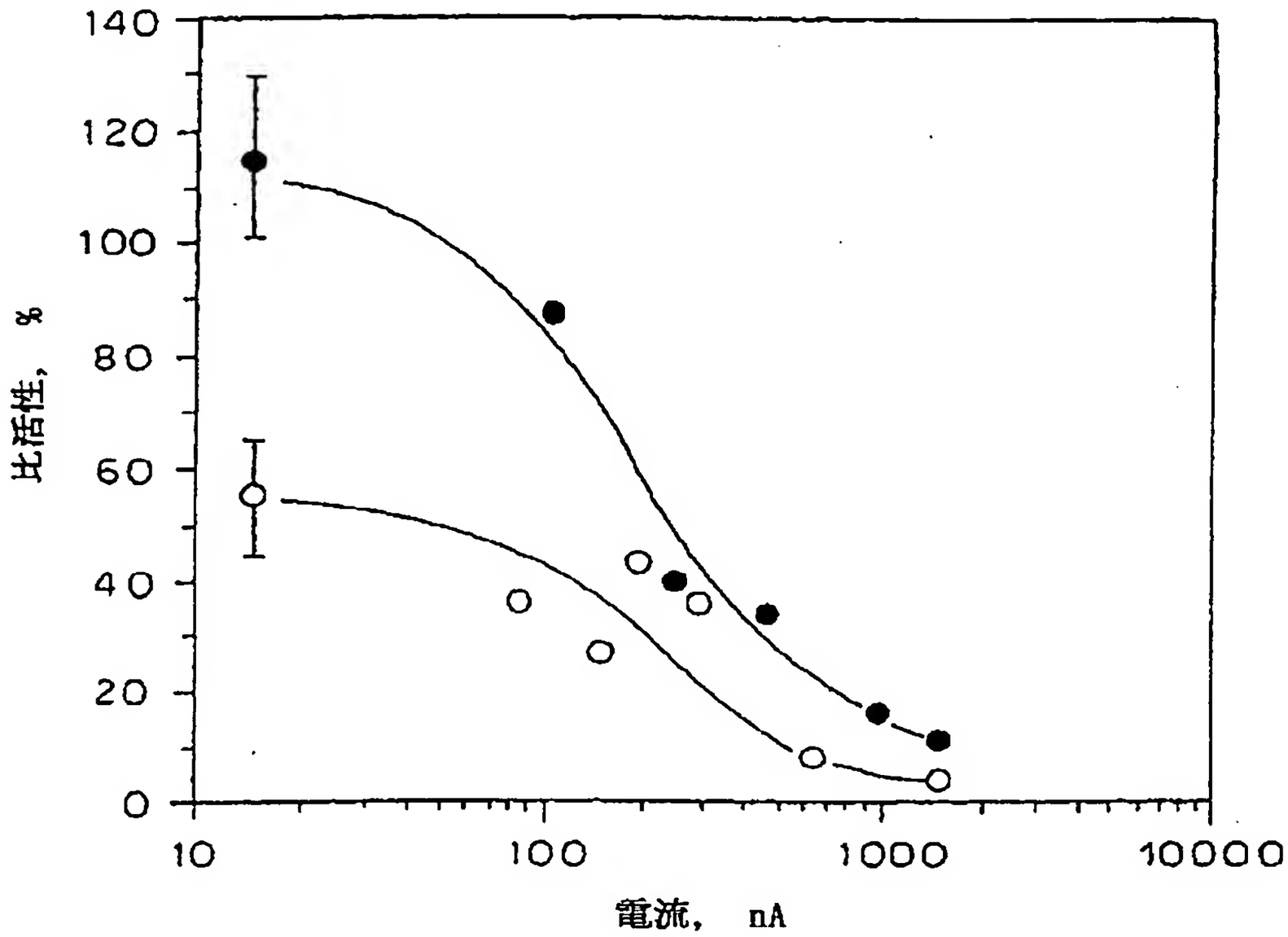
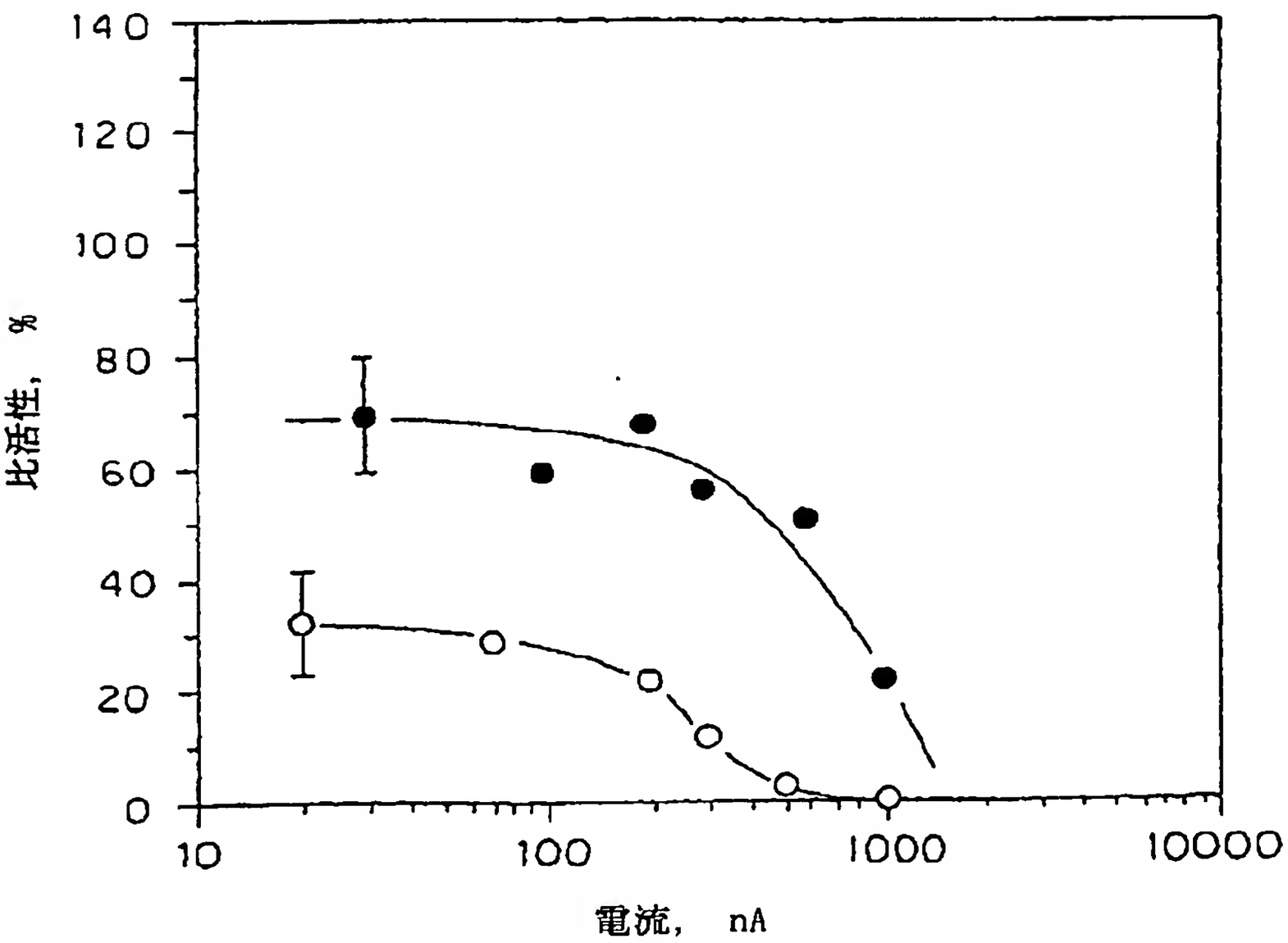
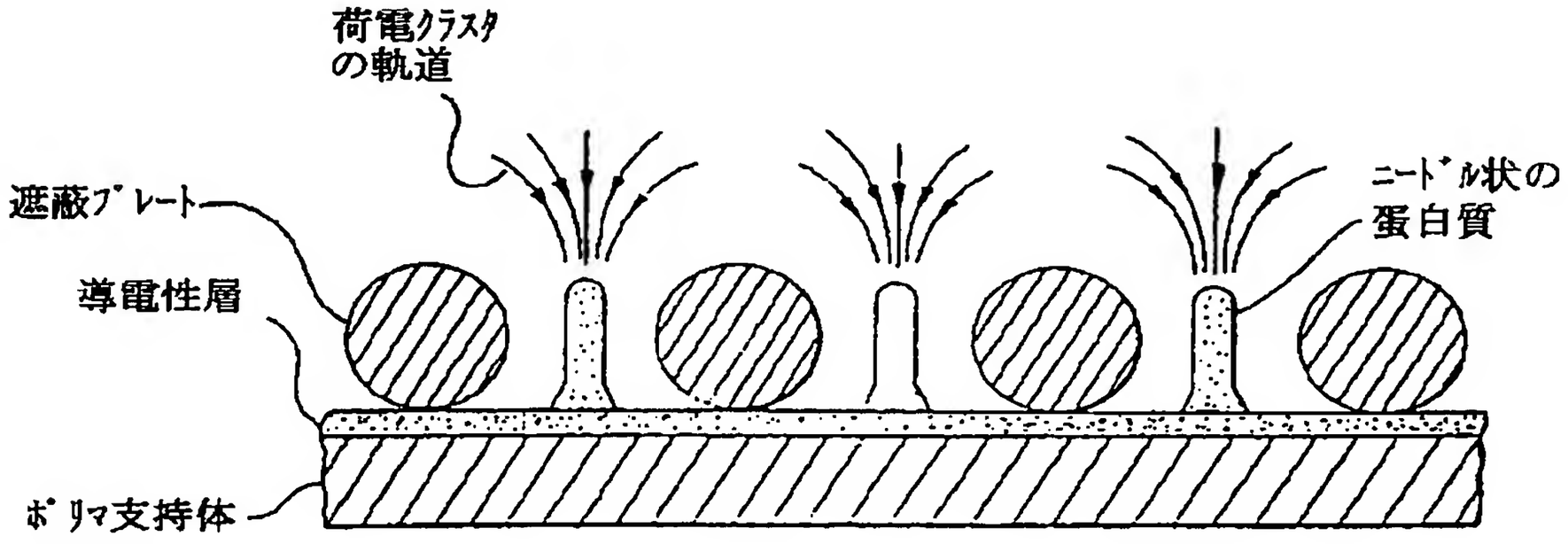


FIG. 18B



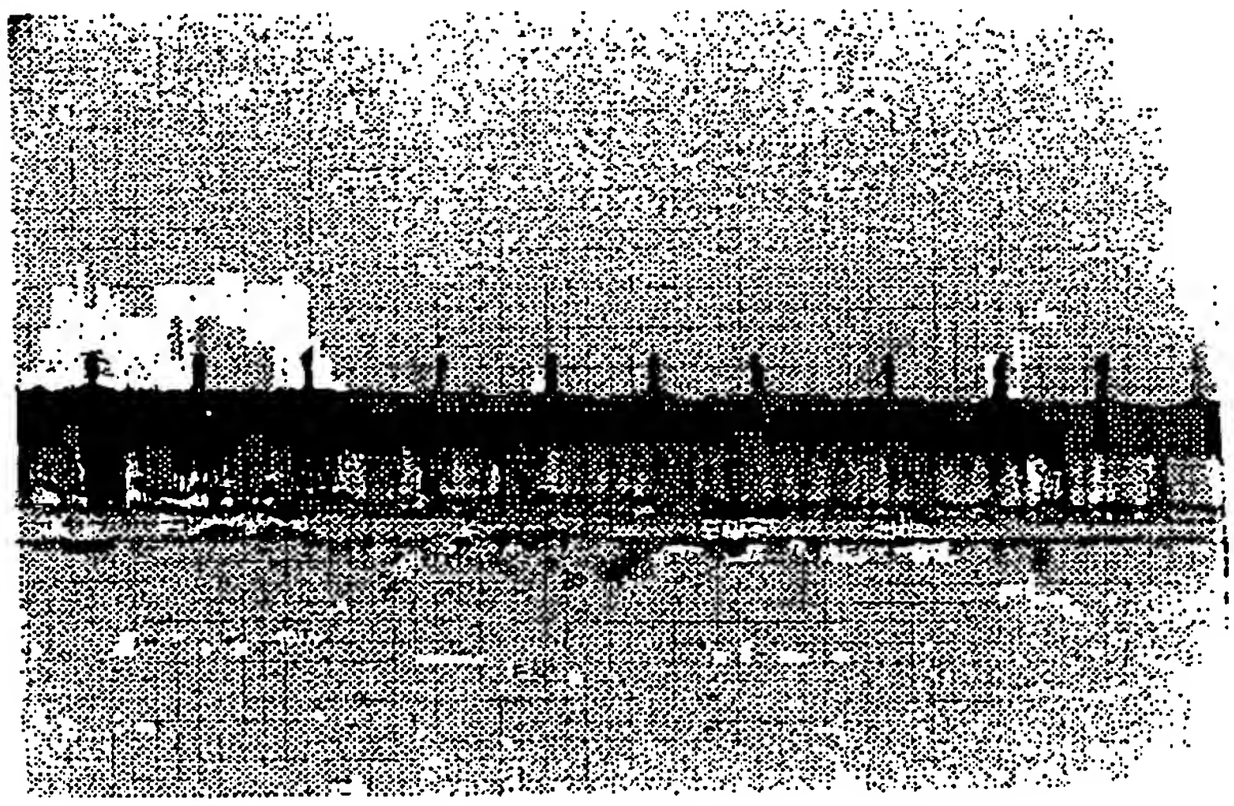
[Drawing 19]

FIG. 19A



[Drawing 19]

FIG. 19B



[Drawing 20]

FIG. 20A

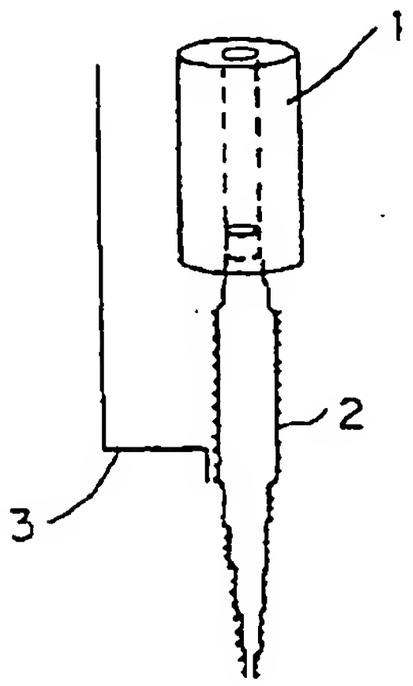


FIG. 20B

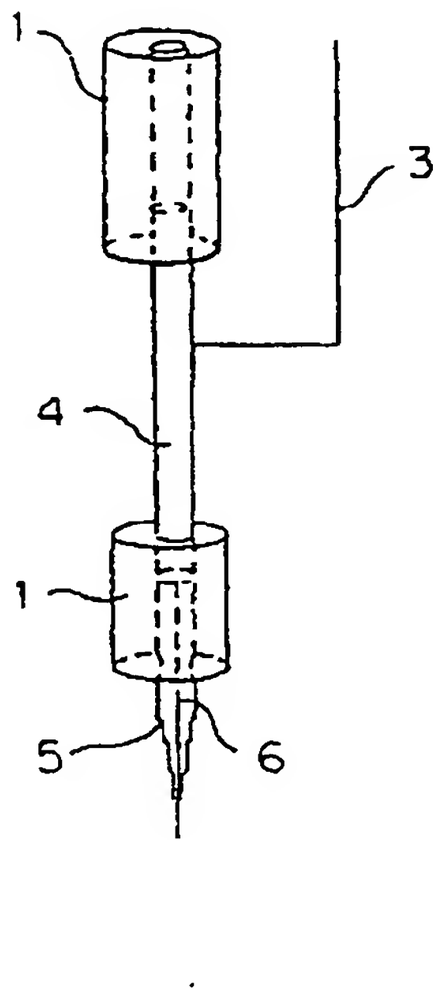
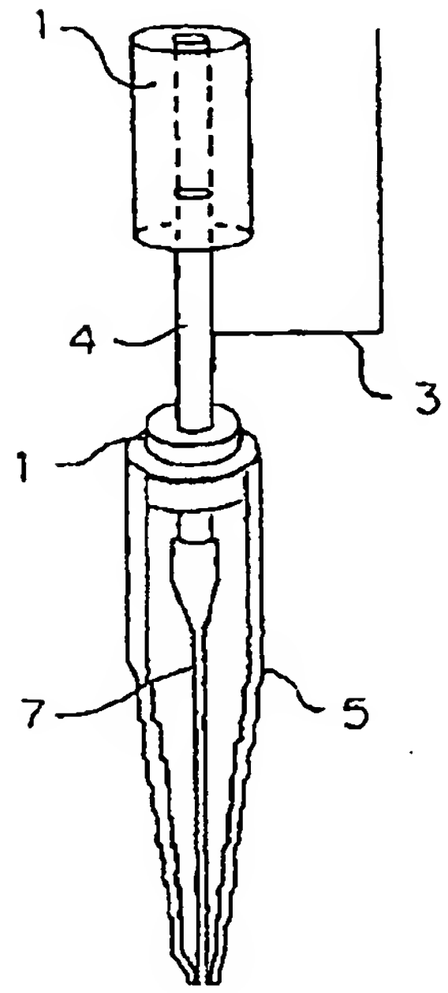


FIG. 20C



[Drawing 21]

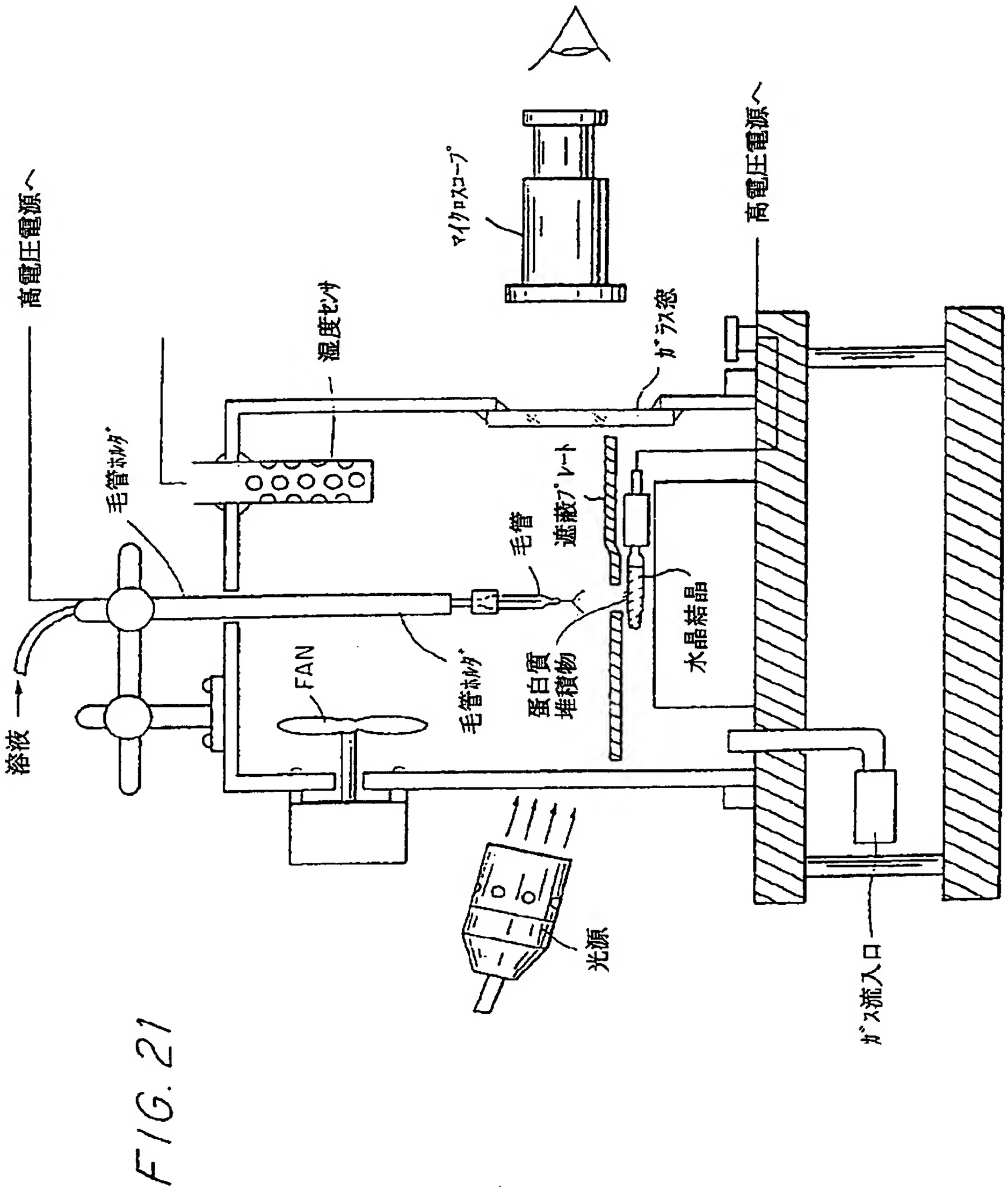
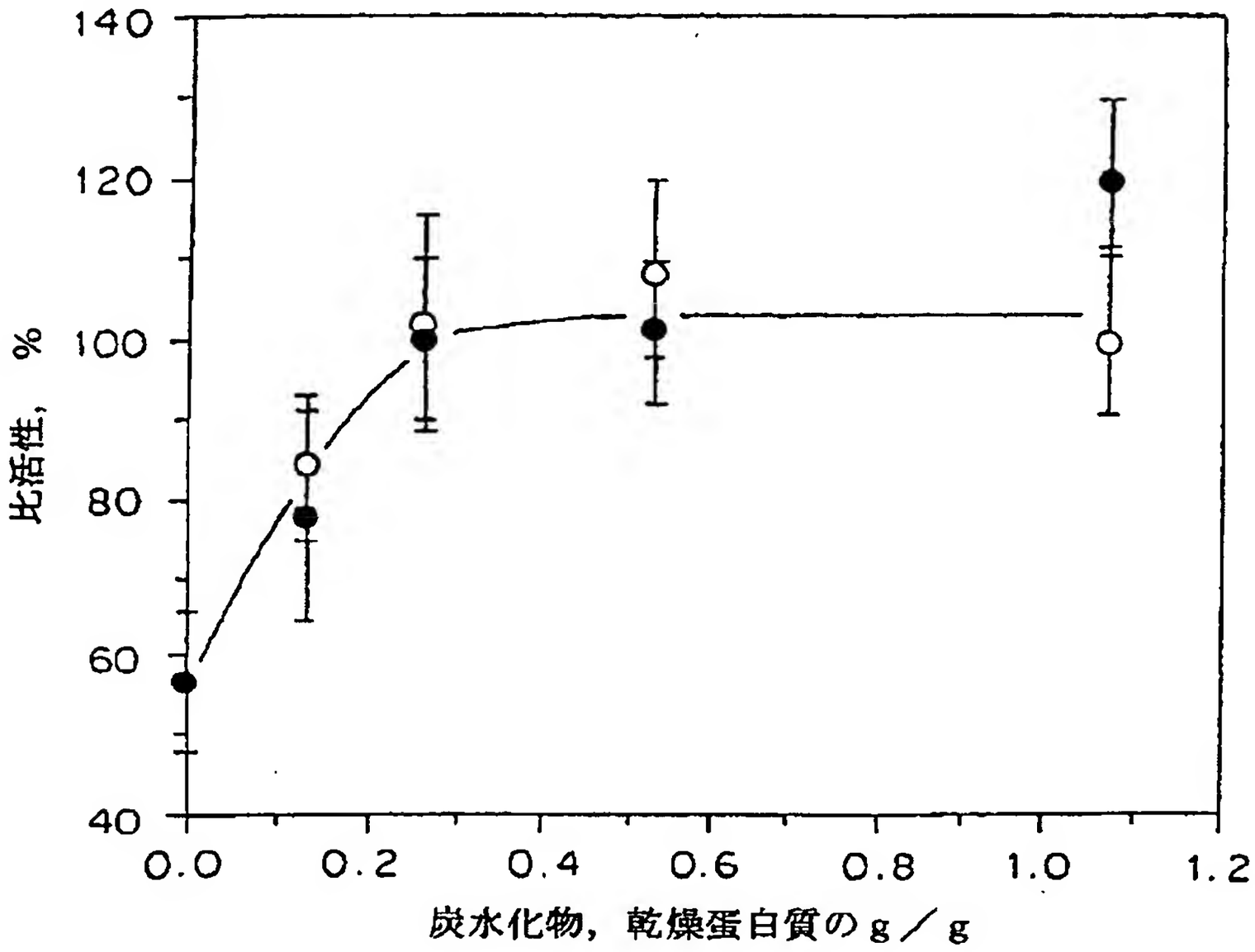


FIG. 21

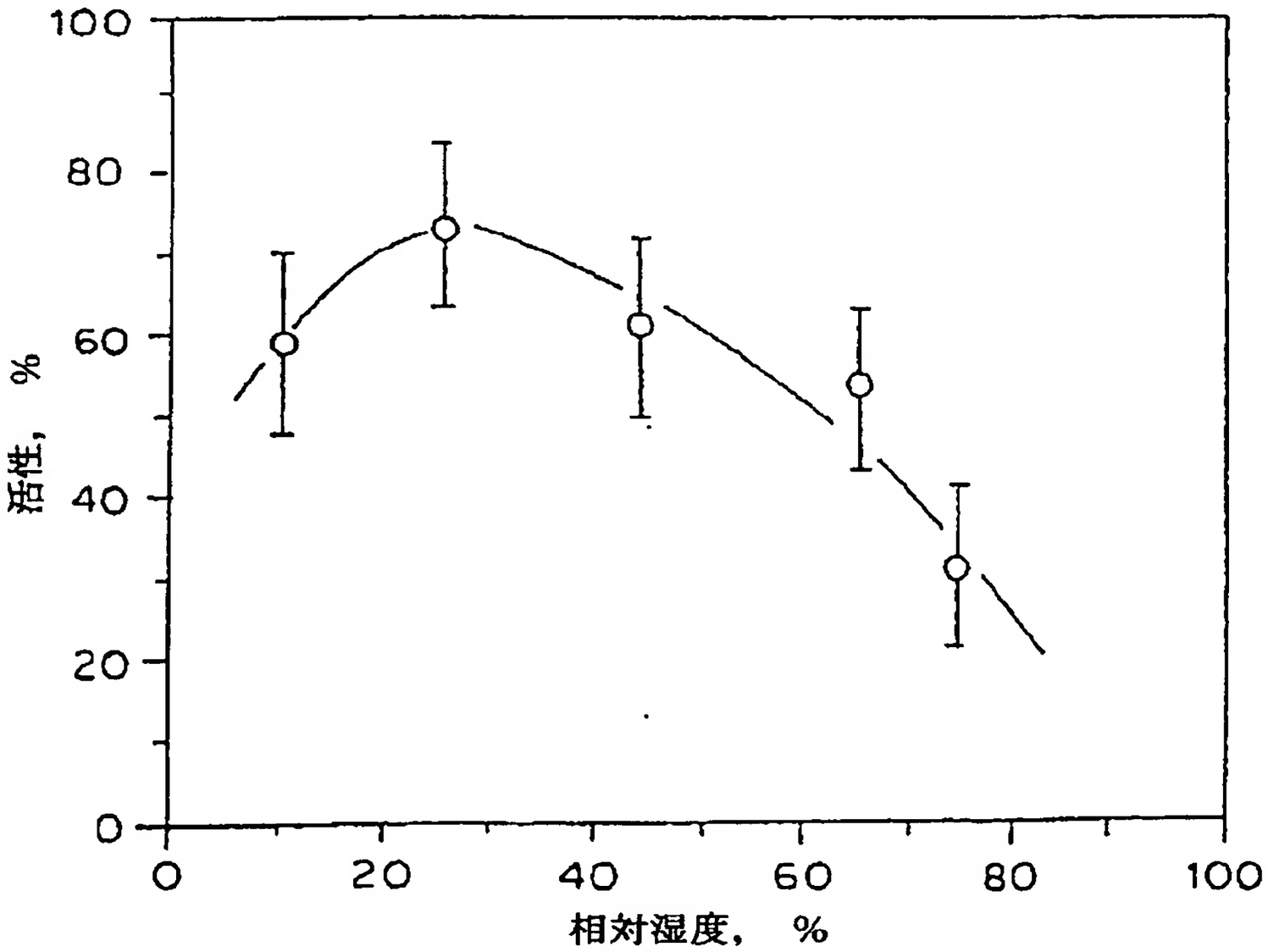
[Drawing 22]

FIG. 22



[Drawing 23]

FIG. 23



[Drawing 24]

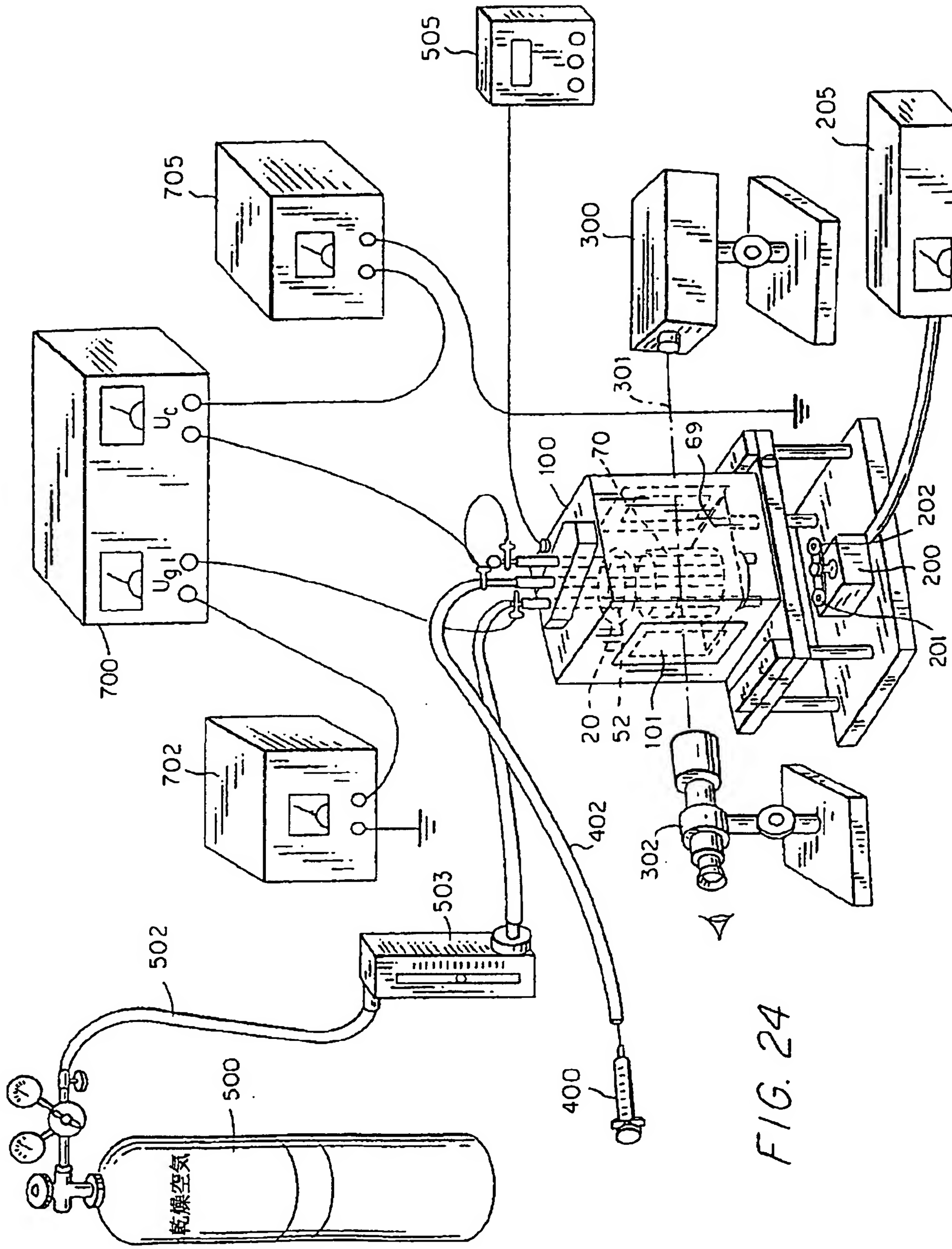
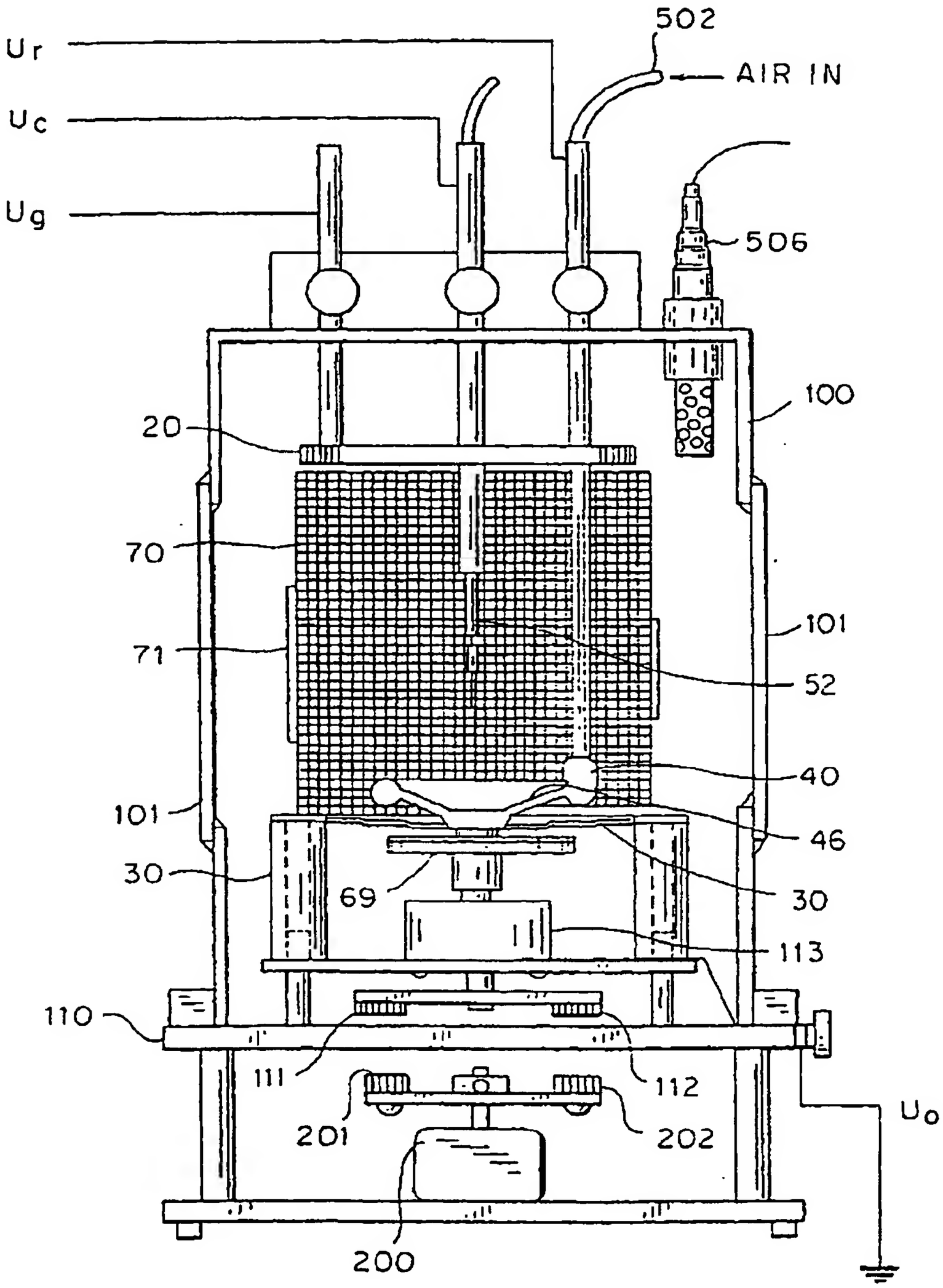


FIG. 24

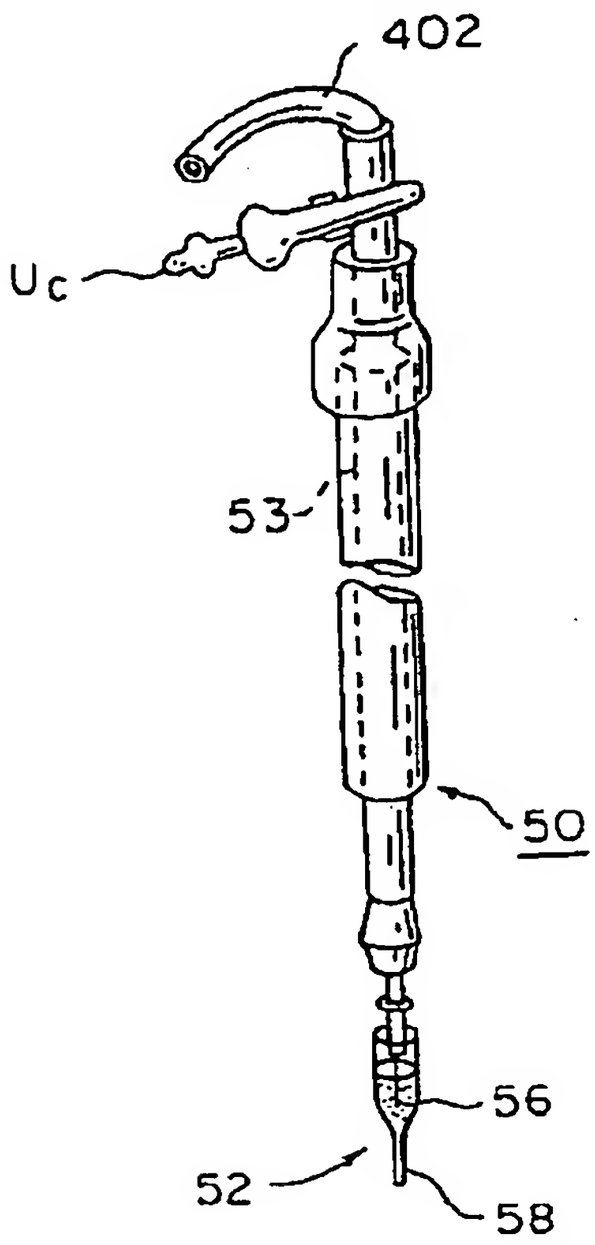
[Drawing 25]

FIG. 25



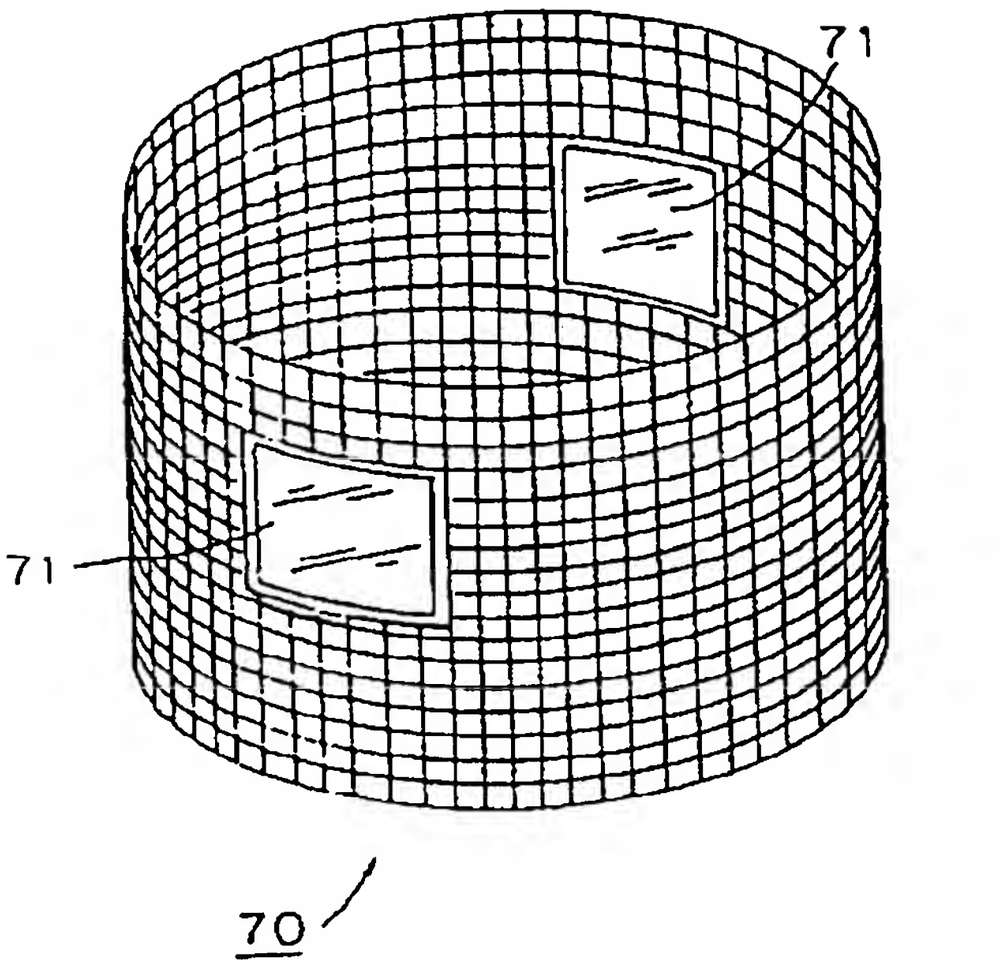
[Drawing 26]

FIG. 26



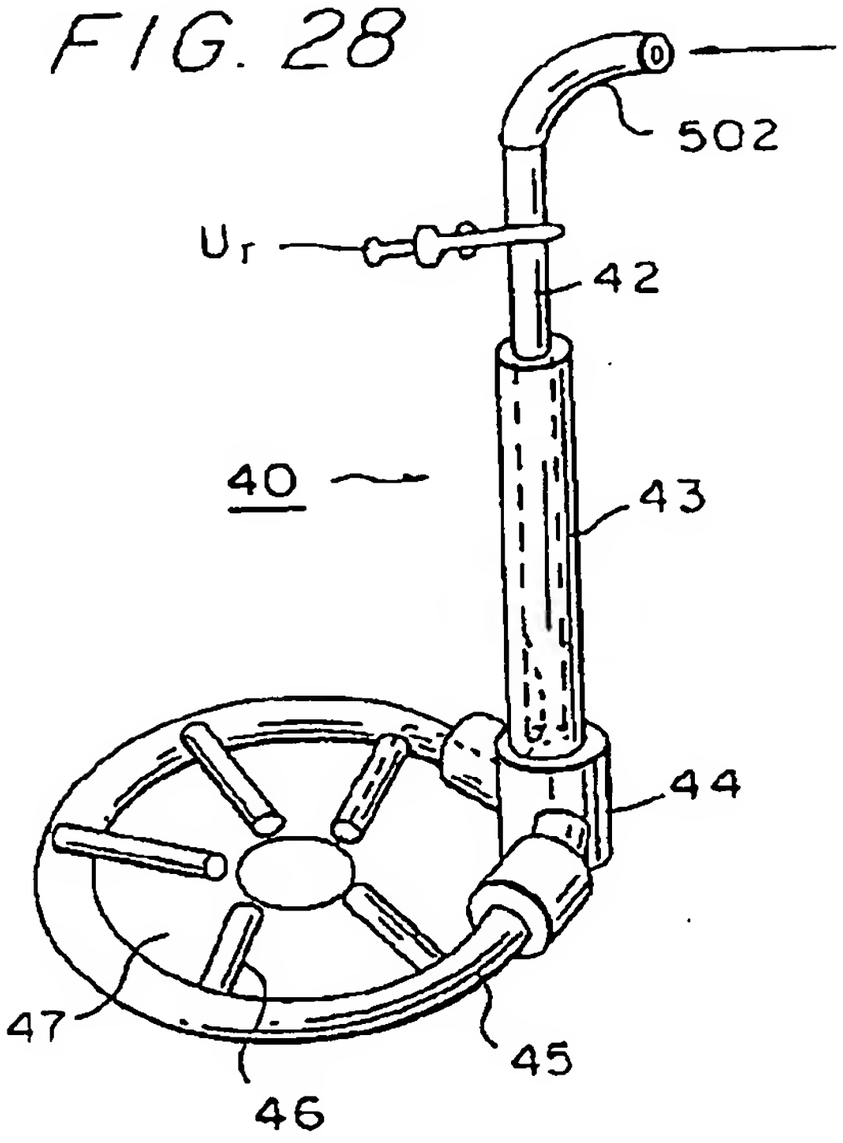
[Drawing 27]

FIG. 27



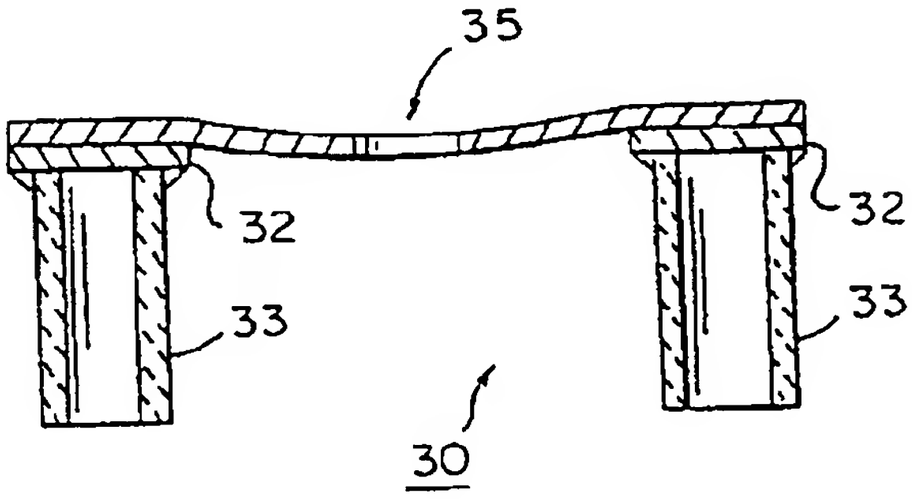
[Drawing 28]

FIG. 28



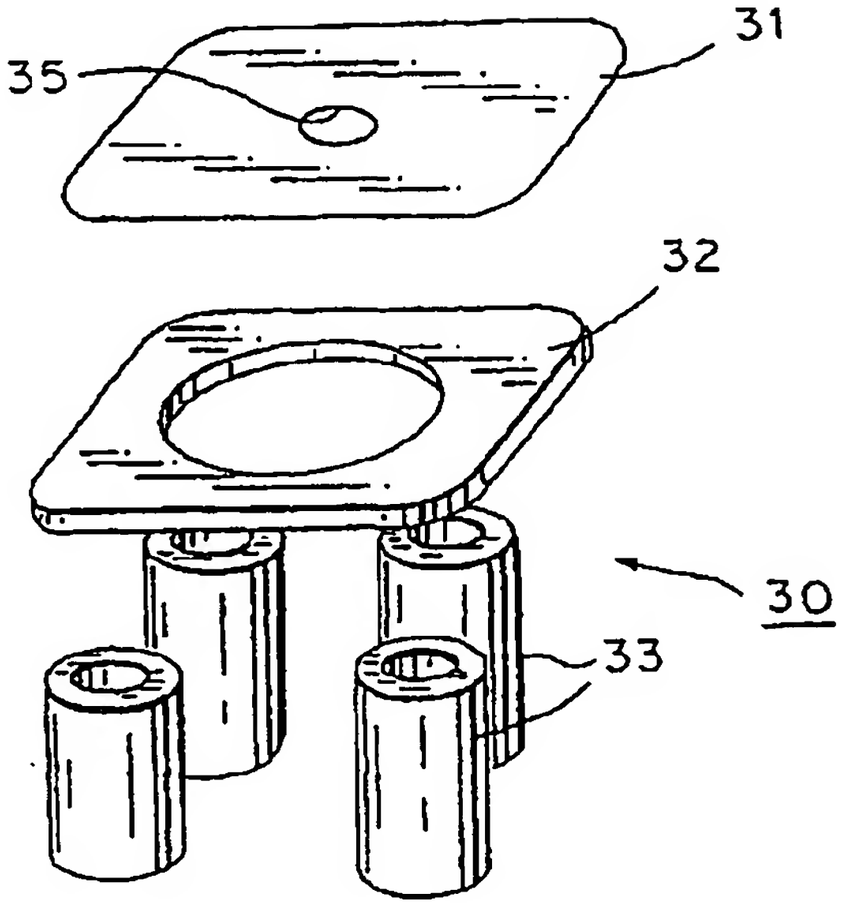
[Drawing 29]

FIG. 29A



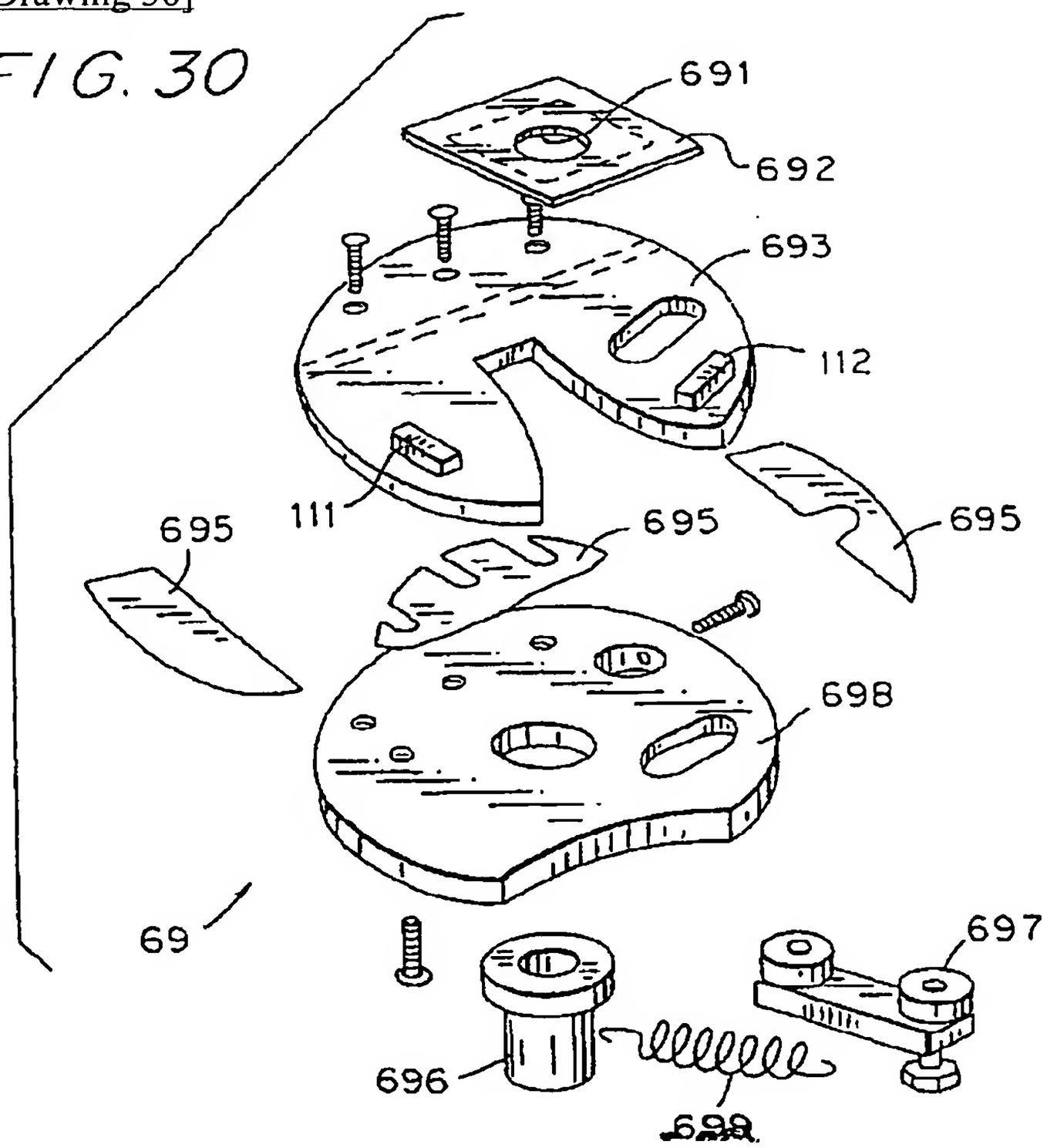
[Drawing 29]

FIG. 29B



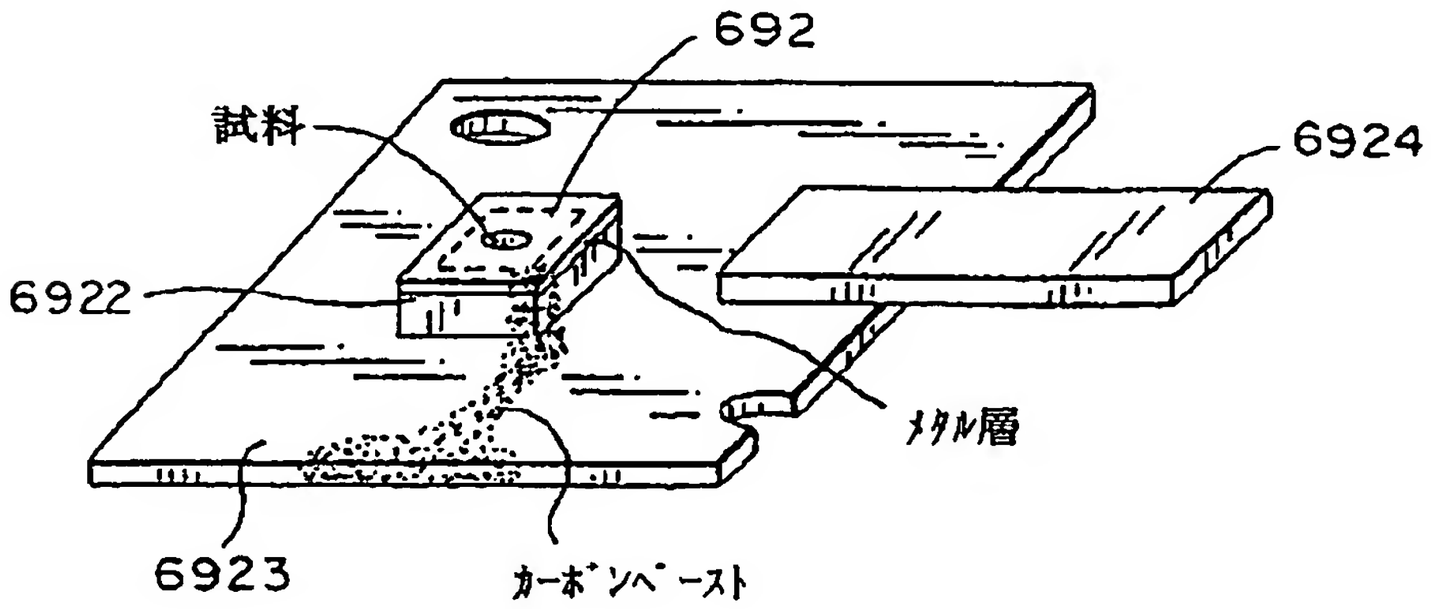
[Drawing 30]

FIG. 30



[Drawing 31]

FIG. 31



[Drawing 32]

FIG. 32A

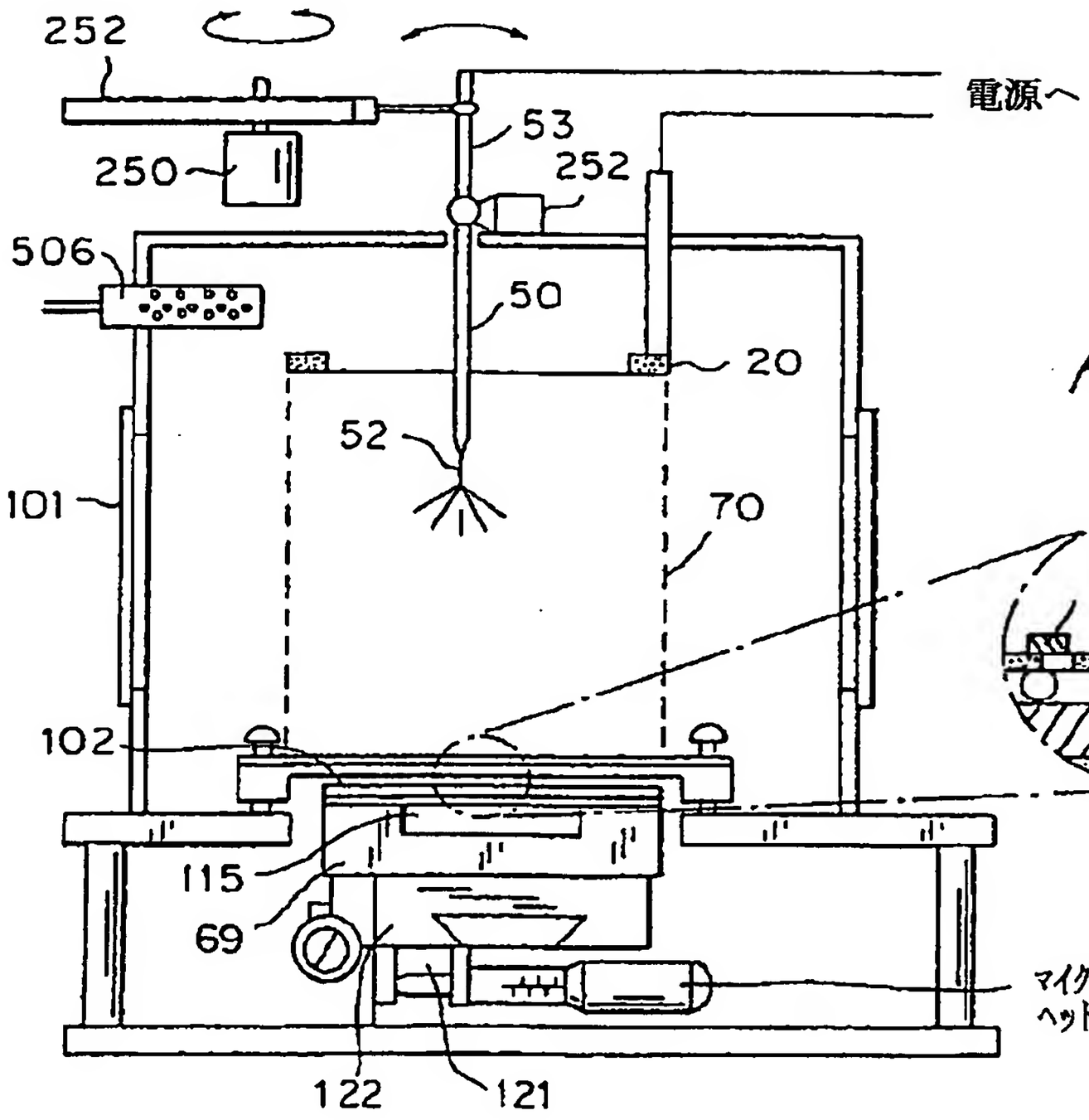
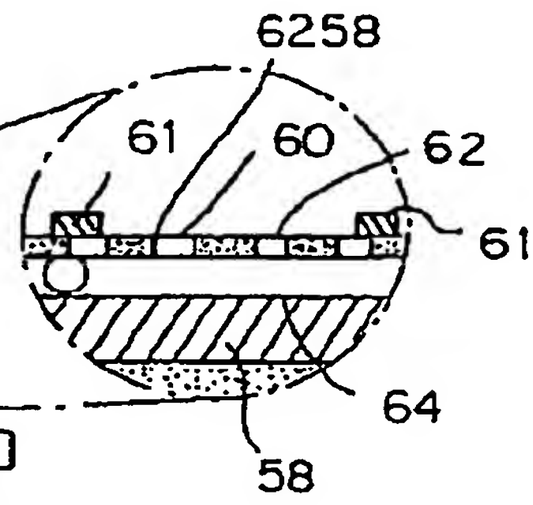
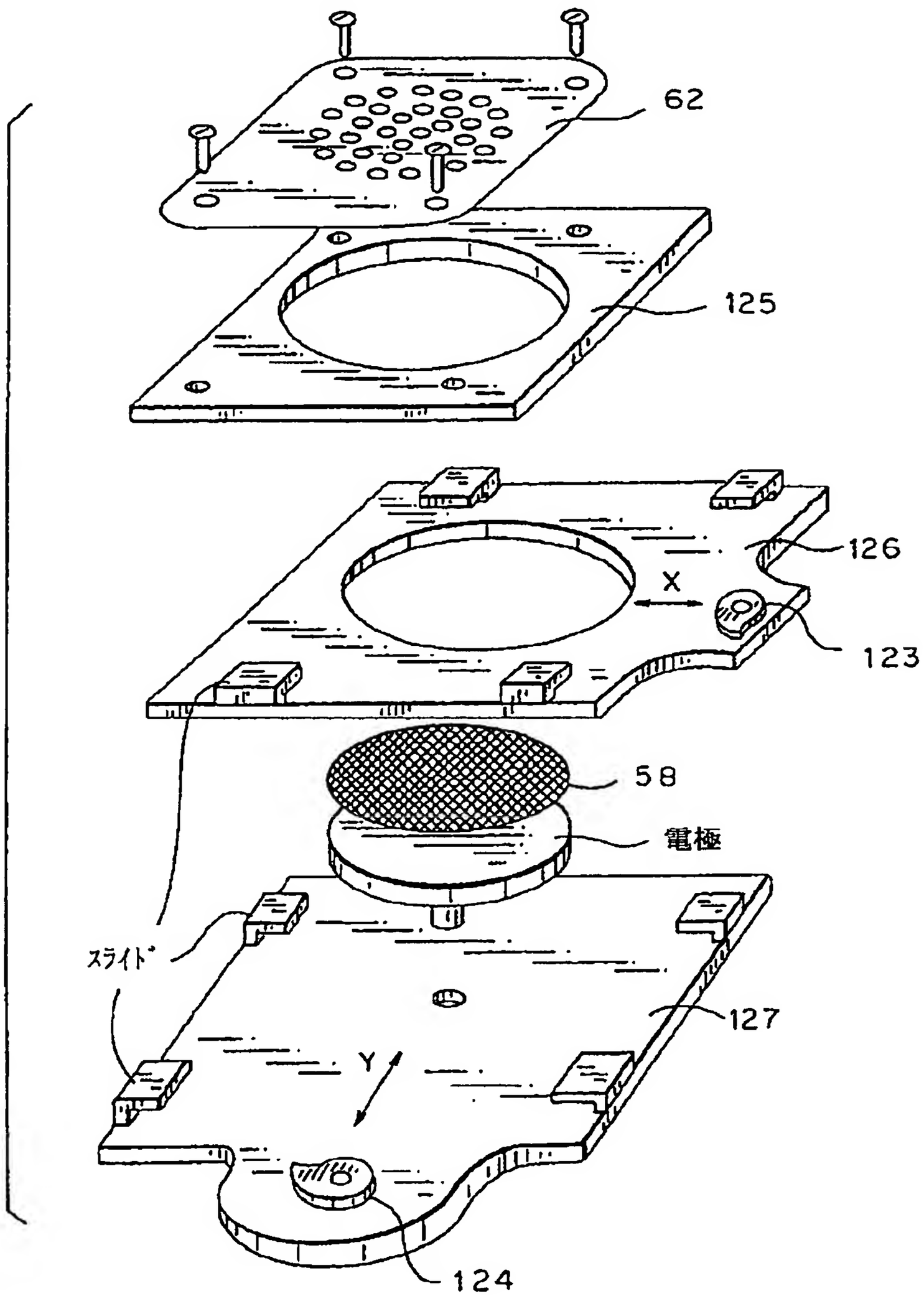


FIG. 32B



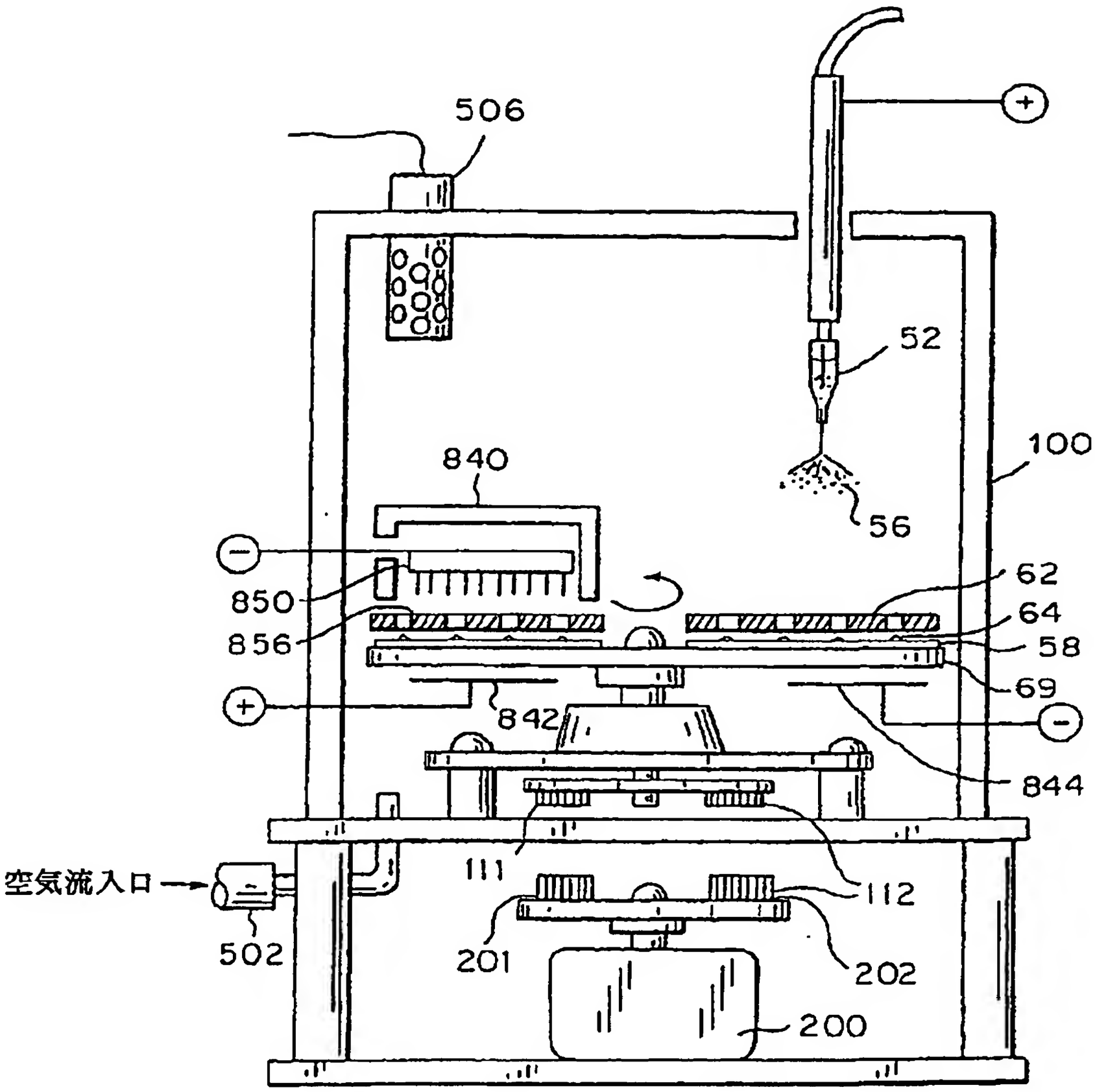
[Drawing 33]

FIG. 33



[Drawing 34]

FIG. 34



[Translation done.]